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- (54) Title: DNA SEQUENCES FOR ENZYMATIC SYNTHESIS OF POLYKETIDE OR HETEROPOLYKETIDE COMPOUNDS
- (54) Titre: SEQUENCES D'ADN DESTINEES A LA SYNTHESE ENZYMATIQUE DE COMPOSES A BASE DE POLYKETIDES OU D'HETEROPOLYKETIDES

(57) Abstract

The invention consists of: (1) cloned Sorangium cellulosum polyketide synthase (PKS) biosynthetic cluster DNA; and (2) the nucleotide sequence and predicted protein coding sequences of the cloned DNA. The invention can be used for, but not limited to: (a) increasing yields of PKS product in Sorangium cellulosum (e.g., by amplification or genetic modification of the epothilone gene cluster or its component parts); (b) increasing yields of polyketide product in a heterologous system by transfer of the epothilone gene cluster or its component parts, which may be followed by amplification or genetic modification of the PKS gene cluster or its component parts; (c) modification of the polyketide product chemical structure in either Sorangium cellulosum or a heterologous host (e.g., by genetic modification of the epothilone gene cluster or its component parts; and (d) for the detection of genes and gene products involved in making polyketides or related molecules in other organisms (e.g., by hybridization or complementation assays). DNA sequence and analysis is presented for the following cosmids and plasmids: A2 cosmid; the pEPOcos6 region (overlapping of pEPOcos6 and pEPOcos7); pEPOcos8 cosmid; A5 cosmid; Sau4 (10 kb plasmid).

(57) Abrégé

L'invention concerne: (1) un ADN biosynthétique cloné en grappe de polykétide synthase (PKS) de Sorangium cellulosum; et (2) la séquence nucléotidique et les séquences protéiques codantes prévues de l'ADN cloné. L'invention peut avoir les applications suivantes (sans caractère limitatif): (a) augmentation de la production de PKS chez Sorangium cellulosum (p.ex., par l'amplification ou la modification génétique de la grappe de gènes épothilone ou de ces parties constitutives); (b) augmentation de la production du produit polykétide dans un système hétérologue par le transfert de la grappe de gènes épothilone ou de ces parties constitutives, qui peut être suivie par l'amplification ou la modification génétique de la grappe de gènes PKS ou des ses parties constitutives; (c) modification de la structure chimique du produit polykétide soit chez Sorangium cellulosum soit chez un hôte hétérologue (p:ex., par l'amplification ou la modification génétique de la grappe de gènes épothilone ou de ces parties constitutives); et (d) détection de gènes et de produits géniques participant à la fabrication de polykétides ou de molécules correspondantes dans d'autres organismes (p.ex., par des dosages à hybridation ou à complémentation). La séquence d'ADN et l'analyse sont présentées pour les cosmides et les plasmides suivants: cosmide A2; région pEPOcos6 (se chevauchant avec pEPOcos6 et pEPOcos7); cosmide pEPOcos8; cosmide A5; Sau4 (plasmide 10 kb).

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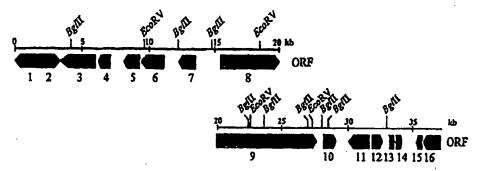
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(54) Title: DNA SEQUENCES FOR ENZYMATIC SYNTHESIS OF POLYKETIDE OR HETEROPOLYKETIDE COMPOUNDS



(57) Abstract

The invention consists of: (1) cloned Sorangium cellulosum polyketide synthase (PKS) biosynthetic cluster DNA; and (2) the nucleotide sequence and predicted protein coding sequences of the cloned DNA. The invention can be used for, but not limited to: (a) increasing yields of PKS product in Sorangium cellulosum (e.g., by amplification or genetic modification of the epothilone gene cluster or its component parts); (b) increasing yields of polyketide product in a heterologous system by transfer of the epothilone gene cluster or its component parts, (c) increasing fields of partyleside product in a increatingous system by training of the epotationing gene cluster or its component parts; (c) modification of the polyketide product chemical structure in either Sorangium cellulosum or a heterologous host (e.g., by genetic modification of the epothilone gene cluster or its component parts; and (d) for the detection of genes and gene products involved in making polyketides or related molecules in other organisms (e.g., by hybridization or complementation assays). DNA sequence and analysis is presented for the following cosmids and plasmids: A2 cosmid; the pEPOcos6 region (overlapping of pEPOcos6 and pEPOcos7); pEPOcos8 cosmid; A5 cosmid; Sau4 (10 kb plasmid).

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DNA sequences for enzymatic synthesis of polyketide or heteropolyketide compounds

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The present invention relates to DNA sequences for enzymatic synthesis of polyketide or heteropolyketide compounds produced by the bacterium Sorangium cellulosum.

15 Background and introduction

This patent application describes DNA sequences for the enzymatic synthesis of polyketide and/or heteropolyketide structures synthesized by the myxobacterium Sorangium cellulosum. Several of these compounds have known cytotoxic, immunosuppressive, antibiotic and fungicidal biological activity, with the epothilones having been most studied and character-The fermentation of large quantities of secondary metabolites from microorganisms, especially from myxobacteria, is a time consuming and difficult process that often involves complications (e.g. contamination, low product yield, difficult isolation and purification). Therefore it would be advantageous to use a well-characterized organism for such fermentations. After cloning of the desired biosynthetic genes one could create such an organism via genetic engineering and manipulate the biosynthesis of the compound. Identified sequences

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can be cloned into optimized expression vectors and generate recombinant cell lines that overproduce polyketide structures.

Polyketide synthases (PKS) and non-ribosomal peptide synthetases (NRPS) represent macromolecular and multifunctional enzymes which are characterized by a modular architecture. PKS condenses activated carbonic acids (usually acetate and propionate) and reduce the resulting 2-keto acid intermediates stepwise in a fatty acid biosynthesis-like fashion. Responsible for each reaction step is a specific domain that recognizes, activates, condenses and reduces the carbonic acid. Depending on the presence of these domains in the corresponding modules, every reduction stage can occur in the final product (Rawlings, Nat. Prod. Reports <u>14</u>, 523-556 [1997]; for a review, see Chem. Rev. <u>97</u>, 2463-2760 [1997]). A typical example for the biosynthesis of a polyketide is the macrolide antibiotic erythromycin (Staunton and Wilkinson, Chem. Rev. 97, 2611-2630 [1997]). NRPSs are also modular enzymes and condense via peptide bonds amino acids to low molecular weight bioactive substances like bacitracin or tyrocidin. Typical domains of these systems activate the amino acid and condense it with the growing peptide chain. Methylations, epimerisations and modifications via additional protein domains are possible (Stachelhaus and Marahiel, FEMS Microbiol Lett. 125, 3-14 [1995]). Both types of enzymes (NRPS and PKS) share the modular organization of the proteins in which specific catalytic domains are responsible for recognition, activation, condensation and modification of the single elongation units. The growing chain of amino acids and/or carbonic acids is extended through the action of one module adding one unit. The domains of each module carry the active centers responsible for the enzymatic steps of the biosynthesis.

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Little is known about the biosynthesis of biologically active polyketides and polypeptides from myxobacteria. Fragments of the biosynthetic gene clusters of soraphen and saframycin have been described from Sorangium cellulosum So ce26 and Myxococcus xanthus, respectively (Schupp et al., J. Bacteriol. 177, 3673-3679 [1995] and Pospiech et al., Microbiology 141, 1793-1803 [1995]). We have constructed genomic libraries of the epothilone producer Sorangium cellulosum So ce90. Gene probes based on PKS and PS genes were used to isolate recombinant cosmids, which were then sequenced and characterized. Several unique pathways containing PKS, PS, or a combination of both types of genes were identified, demonstrating that this organism is potentially a rich source of novel bioactive compounds.

A subject of the present invention is therefore to provide DNA sequences according to claim 1 the expression products of which perform or are involved in the enzymatic biosynthesis, mutasynthesis or partial synthesis of polyketide or heteropolyketide compounds. The DNA sequences may be inserted into well known and optimized expression vectors by commmon techniques of molecular biology, thus allowing transformation, selection and cloning of cells, which cells are then capable of synthezising polyketide or heteropolyketide compounds by fermentation. Using an overproducing clone allows the desired polyketide or heteropolyketide compounds be easily produced and recovered in high amounts. Further, knowledge of the localization of regulatory DNA segments and individual structural genes allows "site-directed mutagenesis" using common techniques for genetic engineering, and thus construction of optimized enzymes ("protein engineering") for fermentative synthesis of polyketide or heteropolyketide compounds.

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The invention thus further relates to a recombinant expression vector according to claim 16, cells transformed therewith according to claim 17 and to a process for enzymatic biosynthesis, mutasynthesis or partial synthesis of polyketide or heteropolyketide compounds according to claim 23.

Preferred and/or advantageous embodiments of the present invention are subject-matter of the subclaims.

In brief, the invention consists of (1) cloned Sorangium cellulosum polyketide synthase (PKS) and/or peptide synthetase (PS) biosynthetic cluster DNA and (2) the nucleotide sequence and predicted protein coding sequences of the cloned DNA. The invention can be used for, but not limited to, (a) increasing yields of PKS product in Sorangium cellulosum (e.g., by amplification or genetic modification of the epothilone gene cluster or its component parts), (b) increasing yields of polyketide and/or peptide synthetase product in a heterologous system by transfer of the corresponding gene cluster or its component parts, which may be followed by amplification or genetic modification of the PKS and/or PS gene cluster or its component parts, (c) modification of the polyketide and/or peptide synthetase product chemical structure in either Sorangium cellulosum or a heterologous host (e.g., by genetic modification of the corresponding gene cluster or its component parts) and (d) for the detection of genes and gene products involved in making polyketides or related molecules in other organisms (e.g., by hybridization or complementation assays). DNA sequence and analysis is presented for the following cosmids and plasmids:

- A2 cosmid as defined in claim 6
- the pEPOcos6 region (overlapping of pEPOcos6 and pEPOcos7)
 30 as defined in claim 7

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10		 pEPOcos8 cosmid as defined in claim 10 A5 cosmid as defined in claim 12 Sau4 (10 kb plasmid) as defined in claim 14
15	5	The invention is now described in more detail by examples an for illustration only. The examples are not to be construed a any limitation of the scope.
20	10	Figure 1 is a restriction map of one of the DNA sequences of the present invention (cosmid A2 insert) indicating also the localization of regulatory DNA segments and the individual structural genes ("open reading frames" or ORFs) 1 to 16.
25	15	Figure 2 shows the open reading frames found on pEPOcos6 region
30		DNA sequence data from A2 cosmid are as defined in claim 6. Table 1 correlates ORFs 1 to 16 found on A2 cosmid with the respective biological function (Regulators, Enzymes).
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Table 1

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	T	
	gene/function	position
1	regulatory element	1666 - 1
2	regulatory element	1605 - 3338
3	acyl-t-RNA synthetase	6100 - 3398
4	monooxygenase	7110 - 6374
5	amino transferase	9590 - 8433
6 	L-dopa decarboxylase	11393 - 9855
7	cxidoreductase	13656 - 12712
8	polyketide synthase	15374 - 18984
9	polypeptide synthetase	20003 - 27889
10	peptidase	28251 - 29402
11	regulatory element	31720 - 30401
12	sigma factor	31982 - 32932
13	regulatory element	33128 - 33613
14	regulatory element	33661 - 34007
15	transcription regulator	35611 - 35255
16	signal transduction	37856 - 35730
	2 3 4 5 6 7 8 9 10 11 12 13 14	regulatory element acyl-t-RNA synthetase monooxygenase L-dopa decarboxylase cxidoreductase polyketide synthase polypeptide synthetase regulatory element regulatory element regulatory element regulatory element regulatory element regulatory element transcription regulator

Working Examples

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- A. Construction of a Sorangium cellulosum cosmid library
- 5 1. Isolation of genomic DNA from S. cellulosum So ce90

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a. Sorangium cellulosum So ce90 was spread onto solid CA-2 agar and incubated at 30° C for 5-7 days. CA-2 agar is prepared by autoclaving 18 g Bacto-agar (Difco Laboratories, Detroit,

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MI) in 800 ml dH₂0 for 20 min at 121°C and cooling to 50-55°C in a water bath. The following filter-sterilized solutions are added to the agar: 20% (w/v) glucose, 50 ml; Solution A (7.5% [w/v] KNO₃,7.5% K₂HPO₄), 10 ml; Solution B (1.5% [w/v] MgSO₄·7H₂O), 10 ml; Solution C (0.2% [w/v]CaCl₂·2H₂O,0.15% [w/v]

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15 FeCl₃), 10 ml; 1 M HCl, 1 ml; autoclaved 4-day old Sorangium cellulosum broth, 100 ml. A sample of cells was removed from the plates with a sterile loop and inoculated into 50 ml of G51t medium in a 250 ml Erlenmeyer flask. G51t consists of 0.5% starch (Cerestar), 0.2% tryptone, 0.1% yeast extract, 0.05%

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CaCl₁, 0.05% MgSO₄ 7H₂O, 1.2% 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES), 0.2% glucose, pH 7.6. The flasks were shaken at 30°C, 160 rpm until a dense orange bacterial growth was obtained (ca. 5-7 d.). The cells were pelleted by centrifugation at 6,000 x g and used immediately or stored fro-

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25 zen at -20°C.

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The protocol used for isolating chromosomal DNA from bacteria using hexadecyltrimethylammmonium bromide (CTAB) has been described previously (Ausubel et al., Current Protocols in Molecular Biology, John Wiley and Sons, New York, 1990). The precipitated DNA was recovered with a bent Pasteur pipette, washed

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with 70% and 95% ethanol, air-dried, and resuspended in 0.5 ml TE buffer (0.01 M Tris-HCl, 0.001 M ethylenediaminotetraacetic acid [EDTA], pH 8.0).

b. Alternatively, genomic DNA was isolated from S. cellulosum cells cultured as described in section A.1 using the Midi Qiagen Blood & Cell Culture DNA purification Kit (Qiagen, Hilden, Germany) following the Qiagen Genomic DNA Handbook protocol for bacterial DNA isolation (1997, Qiagen, Hilden, Germany, p. 29 ff.). In order to obtain high molecular weight chromosomal DNA the precipitated DNA was recovered with a bent pasteur pipette as described in section A.1.

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15 2. Isolation of plasmid DNA

a. pFD666: pFD666 is a bifunctional E. coli-Streptomyces cosmid cloning vector (see Denis and Brzezinski, Gene 111, 115-118 [1992]). To maintain stability of large inserts, it is present in low-medium copy number when replicated in E. coli. For this reason, isolation of sufficient pure DNA to carry out cloning experiments was difficult using commercial kits with standard protocols. A modified procedure was therefore used to obtain pFD666 DNA. A 10 ml culture of DH10B(pFD666) was grown for 16-20 hr at 37°C in LB (1% tryptone, 0.5% yeast extract, 0.5% NaCl, pH 7.0) medium containing 50 μg/ml kanamycin sulfate. Fifty ml of LB + kanamycin was inoculated to a starting OD600 of ca. 0.25 and shaken at 300 rpm, 37°C, until the OD600 reached ca. 0.6. Five hundred ml of LB + kanamycin medium in a 2 1

flask was inoculated with 25 ml of this culture and incubated

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under the same conditions for 2.5 hr. Chloramphenicol (2.5 ml of a 34 mg/ml solution in 100% EtOH) was added and the incubation continued for an additional 16-20 hr. (The previous steps were performed according to Maniatis et al. Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1989.) Cells were pelleted for 10 min, 16,000 \times g . They were resuspended in 9 ml of 50 mM glucose/25 mM Tris-HCl (pH 8.0)/10 mM EDTA and transferred to a 50 ml disposable centrifuge tube. One ml of a freshly-prepared 10 mg/ml lysozyme solution in 10 mM Tris-HCl, pH 8.0 was added and the cell sus-10 pension incubated in a 37°C water bath for 10 min. Twenty ml of a freshly-prepared 0.2 NaOH/1% sodium dodecyl sulfate (SDS) solution was added and the tube inverted gently 5-7 times to mix the contents. After 5 min at room temperature, 15 ml of 5 M po-15 tassium actate (pH 4.8) was added and the tube inverted sharply 3-4 times. The tube was centrifuged at 6,000 $extbf{x}$ g for 10 min at $4^{\circ}\mathrm{C}$ and the supernatant poured though 2 layers of sterile cheese cloth into a fresh 50 ml disposable tube. Isopropanol to a final concentration of 0.6% was added and the contents of the tube mixed several times. The precipitated nucleic acid was centrifuged at 6,000 x g for 10 min at 4°C. The pellet was washed with 70% EtOH and any excess EtOH was aspirated from the pellet, which was allowed to air dry for 5 min. It was resuspended in 5 ml of 50 mM 3-(N-Morpholino)propanesulfonic acid (MOPS)/750 mM NaCl, pH 7.0 and added to an equilibrated to 25 QIAfilter Midi column (Qiagen, Chatsworth, CA). The manufacturer's protocol for washing and eluting the plasmid DNA was followed.

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b. SuperCos: SuperCos plasmid DNA was purchased from Stratagene (La Jolla, CA).

3. Preparation of ca. 38-47 kb Sau3Al fragments of S. cellulosum chromosomal DNA

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a. S. cellulosum chromosomal DNA prepared as described in section A.1.a was partially cleaved with restriction endonuclease Sau3A1 in a 1000 μl reaction volume consisting of 50 μg chromosomal DNA, 5 units enzyme (Promega, Madison , WI), 0.006 M Tris-HCl, 0.006 M MgCl₂, 0.10 M NaCl, and 0.001 M dithiothreitol (pH 7.5) for 5 min at 37°C. The reaction mixture was extracted once with an equal volume of 1:1 phenol:chloroform. After centrifugation, the upper aqueous phase was saved, to which 0.1 vol. of 3 M sedium acetate and 0.6 vol. isopropanol was added. DNA was pelleted by centrifugation for 5 min at 16,000 x g in a microfuge and washed once with 0.5 ml 70% EtoH. After drying in a SpeedVac (Savant Instruments, Farmingdale, NY) for 5 min, the pellet was resuspended in 0.1 ml TE buffer.

The DNA was layered ontop of a 12 ml 10-40% sucrose gradient

prepared in TE buffer and centrifuged at 113,600 x g for 16 hr,

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10°C using a Beckman SW40Ti rotor (Beckman Instruments, Palo Alto, CA). Five hundred μl aliquots of the gradient were removed using a pipetor beginning at the top of the tube. Samples
(5 μl) of the fractions were analyzed by electrophoresis through a 0.5% agarose gel in TAE buffer (0.04 M Trizma base, 0.02 M acetic acid, and 0.001 M EDTA, pH 8.3) containing 0.5

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DNA fragments of ca. 40-45 kb were identified by comparison to a high molecular weight DNA standard (Life Technologies,

 $\mu g/ml$ ethidium bromide for 6 hr at 100 V. Fractions containing

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Gaithersburg, MD). Sucrose was diluted from the corresponding 0.5 ml fraction by addition of 0.5 vol. TE. Subsequently, DNA was precipitated by addition of 0.1 vol. 3 M sodium acetate and 0.6 vol. isopropanol. DNA was pelleted by centrifugation at 16,000 x g for 10 min in a microfuge. DNA was washed with 0.5 ml 70% EtOH and dried in a SpeedVac with moderate heat for 10 min. Finally, the DNA was resuspended in distilled $\rm H_2O$ at a concentration of 0.5 mg/ml.

b. Alternatively, 10 μg of S. cellulosum chromosomal DNA pre-10 pared as described in A.1.b was treated with 0.3 U Sau3Al (New England Biolabs, Beverly, MA) for 1 h at 37°C in 400 μ l of the supplier's recommended reaction buffer. Formation of DNA fragments of about 40 kb in size was checked by comparison of the motility behavior with high molecular weight DNA standards af-15 ter a 0.3% agarose gel electrophoresis. An equal volume of phenol:chloroform (1:1) was added, mixed and centrifuged. The upper aqueous phase was recovered and 0.1 vol. of 3 M sodium acetate and 0.6 vol. of isopropanol were added. After centrifuga-20 tion, the precipitated DNA was washed twice with 0.5 ml 70% ice cold ethanol and finally air-dried. The DNA fragments were resuspended in 100 μ l shrimp alkaline phosphatase reaction buffer and dephosphorylated for 150 min. at 37°C using 2 U shrimp alkaline phosphatase (Amersham Life Science, Cleveland, OH). A 25 phenol:chloroform extraction followed as described above. Finally, the DNA was precipitated by addition of 0.1 vol. 3 M sodium acetate and 0.6 vol. isopropanol, dried, and dissolved in

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TE buffer.

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4. Preparation of cosmid libraries

Using pFD666: Vector pFD666 was cleaved with restriction endonuclease BamHI in a 0.02 ml reaction volume consisting of 2 $\mu\mathrm{g}$ plasmid DNA, 10 units of BamHI (Promega), 0.006 M Tris-HCl, 0.006 M MgCl $_2$, 0.05 M NaCl, and 0.001 M dithiothreitol (pH 7.5) for 90 min at 37°C . Five, μl of 10x alkaline phosphatase buffer (0.5 M Tris-HCl [pH 9.3], 0.01 M MgCl₂, 0.001 M ZnCl₂, 0.01 M spermidine) was added to the reaction followed by alkaline phosphatase (0.01 units/pmol ends; Promega) and distilled ${\rm H}_2{\rm O}$ to a final volume of 0.05 ml. The sample was incubated for 30 min at 37°C and a second aliquot of phosphatase was added. After a further 30 min at 37°C , 0.3 ml of stop buffer (0.01 M Tris-HCl [pH 7.5], 0.001 M EDTA, 0.2 M NaCl, 0.5% SDS) and 0.35 ml of 1:1 phenol; CHCl3 was added to the reaction. The sample was mixed gently several times by inversion and centrifuged at 16,000 x g for 3 min to separate the phases. The aqueous layer was removed to a new microfuge tube. 0.1 vol. 3 M sodium acetate and 2 vol. 100% EtOH were added and the precipitated DNA pelleted by centrifugation at 16,000 x g for 10 min. Liquid was removed by aspiration and the pellet washed once with 0.5 ml 70% EtOH. The DNA was dried in a SpeedVac and resuspended in TE buffer to 0.5 mg/ml.

Digested, phosphatase-treated pFD666 was ligated to the partially-cleaved chromosomal DNA (see sections A.3.a and B.1.a) in a 0.005 ml reaction consisting of 1 μ g pFD666, 1 μ g S. cellulosum DNA, 0.03 M Tris-HCl (pH 7.8), 0.01 M MgCl₂, 0.01 M dithiothreitol, and 0.0005 M adenosine-5'-triphosphate and 1.5 Weiss units of T4 DNA ligase (Promega). The reaction was carried out at room temperature for 2 hr. The entire reaction

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mix was packaged into bacteriophage λ in vitro using Packagene extracts (Promega) according to the manufacturer's directions. The entire packaging reaction (0.5 ml) was diluted with 4.5 ml SM buffer (per liter: 5.8 g NaCl, 2 g MgSO $_4$.7 H_2 0, 1 M Tris-HCl[pH 7.5], 5 ml 2% gelatin solution). Transfection was performed by adding 10 ml of an overnight culture of $E.\ coli$ DH5lphathat had been grown in LB medium with 0.01 M MgSO4 and 0.2% maltose to the diluted phage and incubating at 37°C for 20 min. 0.8 ml of LB was added and the cells shaken at 225 rpm for 1 hr 10 at 37°C. Cells were pelleted, resuspended in LB, and spread onto a 150 mm LB + kanamycin agar plate. After 3 d. at 30°C, the colonies were harvested by picking ca. 800 colonies into 2.0 ml LB + kanamycin medium containing 20% glycerol, freezing on dry ice, and storing at -70°C. In addition, six kanamycin-15 resistant colonies were inoculated into 2 ml LB + kanamycin liquid medium and incubated at 37°C, 250 rpm, for 18-24 hr. Cosmid DNA was prepared using a standard alkaline lysis procedure starting with 1.5 ml of the culture. DNA was digested with restriction endonuclease PstI and samples electrophoresed on a 0.8% TAE agarose gel for 1.5 hr at 100 V. A unique restriction 20 pattern was noted in each sample and the total size of the insert was calculated to be between 40 and 45 kilobases.

b. Using SuperCos: 30 μ g of vector SuperCos was digested with XbaI (New England Biolars, Beverly, MA) for 210 min at 37°C in 100 μ l of the recommended reaction buffer. Ten μ l sodium acetate and 60 μ l isopropanol was added before the solution was centrifuged for 30 min at 16,000 x g. The precipitated DNA was washed twice with 500 μ l ice cold 70% ethanol. The vector DNA was precipitated and air-dried, dissolved in 135 μ l shrimp al-

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kaline phosphatase reaction buffer and treated with 2.5 U shrimp alkaline phosphatase for 150 min. After heat inactivation of the enzyme at 75°C for 20 min, a phenol:chloroform extraction was performed as described in section 1. c. The DNA, resuspended in 100 μ l BamHI restriction buffer was hydrolyzed with 15 U BamHI (New England Biolabs, Beverly, MA) for 180 min. A phenol:chloroform extraction followed (see section A.3). The SuperCos DNA was precipitated by addition of 0.1 vol 3 M sodium acetate and 0.6 vol isopropanol, centrifuged at 16,000 x g, and resuspended in 50 μ l TE cuffer.

Four µg of digested vector DNA was ligated with 10 µg partially hydrolyzed genomic DNA from S. cellulosum (as described in section A.3.b) in a final volume of 20 μ l using 2 U T4 DNA ligase and the appropriate reaction buffer (Gibco BRL, Eggenstein, Germany). The reaction was carried out at 16°C overnight. The reaction mixture was packaged into phage particles using the Gigapack III XL packaging extract kit (Stratagene) according to the manufacture's protocol. Treatment of packaging reaction mixture and transfection of E. coli SURE (Stratagene) was performed as described in 4.a. Transfected cells were concentrated by centrifugation, resuspended in fresh LB medium and distributed on LB agar plates containing 50 $\mu g/ml^{-1}$ kanamycin. The plates were incubated overnight at 30°C. 1600 recombinant clones were transferred into 96 well microtiter plates filled with 80 μ l LB medium containing 50 μ g/ml kanamycin per well and propagated overnight at 30°C. The following day the microtiter plates were used to inoculate a second set of microtiter plates in order to obtain a duplicate of the recombinant clones. Each well of the original set of microtiter plates was supplemented with 80 μl 50 % glycerol and the entire plate stored at -70°C.

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20 randomly chosen transformants were inoculated into 3 ml LB medium with 50 $\mu g/ml^{-1}$ kanamycin and incubated over night at 37°C in order to isolate plasmid DNA using the Qiagen plasmid extraction kit (Qiagen, Hilden, Germany). Restriction fragment analysis of the recombinant cosmids using the restriction endonucleases PstI and BglII indicated that the cosmids contained inserts of approximately 35 to 42 kb in size.

B. Construction of a S. cellulosum plasmid library

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1. Preparation of 8-12 kb fragments of S. cellulosum chromosomal DNA.

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S. cellulosum chromosomal DNA prepared as described in section A.1.a was partially cleaved with restriction endonuclease Sau3Al in a 100 μL reaction volume consisting of 5 μg chromosomal DNA, 5 units enzyme (Promega, Madison , WI), 0.006 M TrisHCl, 0.006 M MgCl₂, 0.10 M NaCl, and 0.001 M dithiothreitol (pH 7.5) for 4 min at 37°C. The digested DNA was electrophoresed through a 11 x 14 cm 0.8% TAE-agarose gel for 18 hr at 17 V. Fragments of 8-12 kb were cut from the gel and purified using the QIAquick Gel Extraction Kit using the manufacturer's protocol (Qiagen).

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25 2. Preparation of the plasmid library

Plasmid pZero2.1 (Invitrogen, Carlsbad, CA) was cleaved with restriction endonuclease BamHI in a 0.02 ml reaction volume consisting of 1 μ g plasmid DNA, 10 units of BamHI (Promega), 0.036 M..Tris-HCl, 0.006 M MgCl₂, 0.05 M NaCl, and 0.001 M di-

thiothreitol (pH 7.5) for 20 min at 37°C. 0.08 ml of dH₂O and 0.1 ml of 1:1 phenol:CHC13 was added. The sample was briefly vortexed and centrifuged at 16,000 x g for 2 min. The aqueous layer was removed to a new microfuge tube. 0.1 vol. 3 M sodium acetate and 2 vol. 100% EtOH were added and the precipitated DNA pelleted by centrifugation at 16,000 x g for 10 min. Liquid was removed by aspiration and the pellet washed once with 0.5 ml 70% EtOH. The DNA was dried in a SpeedVac and resuspended in TE buffer to 0.004 μ g/ml. Digested pZero2.1 was ligated to the partially-cleaved chromosomal DNA in a 0.01 ml reaction consisting of 0.004 µg pZero2.1, 0.05 µg S. cellulosum DNA, 0.03 M Tris-HCl (pH 7.8), 0.01 M MgCl₂, 0.01 M dithiothreitol, and 0.0005 M adenosine-5'-triphosphate and 1.5 Weiss units of T4 DNA ligase (Promega). The reaction was carried out at room temperature for 2 hr. 0.015 ml dH_2O and 0.25 ml of 1-butanol were 15 added, the sample vortexed briefly, and centrifuged at 16,000 ${\sf x}$ g for 10 min. Liquid was aspirated away from the pellet and the sample dried in a SpeedVac for 5 min. The ligated DNA was resuspended in 0.005 ml dH2O and mixed with 0.04 ml of electrocompetent Escherichia coli DH10B cells (GIBCO/BRL, Gaithersburg, MD). The sample was placed into a pre-chilled 0.2 mm-gap electroporation cuvette and transformed into the bacteria by electroporation using a BioRad Gene Pulser II unit (BioRad, Hercules, CA) at 25 μF and 200 $\Omega.$ 0.96 ml SOC medium (0.5% yeast extract, 2% tryptone, 10 mM NaCl, 2.5 mM KCl, 10 mM $MgCl_2$, 20 mM $MgSO_4$, 20 mM glucose) was mixed with the cells and transferred to a 1.5 ml microfuge tube. The sample was incubated at 37°C, 225 rpm, for 1 hr. Aliquots of the cells were spread onto an LB agar + kanamycin and incubated at 37°C for 20 hr to estimate the number of transformants obtained. Six kana-

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agar + kanamycin.

mycin resistant colonies were confirmed to contain an insert of the expected size as described in section A.4.a.

C. Identification of cosmids possessing polyketide synthase genes

1. Colony blot hybridizations using cosmid library in pFD666:

A 20 x 20 cm sheet of Duralon UV membrane (Stratagene) was placed on top of a 24.5 x 24.5 cm square bioassay dish containing 250 ml LB agar - kanamycin. An aliquot of the frozen cosmid library in 1 ml LE medium was spread on the filter. The plate was incubated at 37°C for 24 hr. Colonies were replicated onto two fresh filters which were placed onto LB + kanamycin agar medium and incubated at 28°C for 18 hr. Lysis of cells and neutralization of released DNA was performed according to directions that were provided with the filters. The DNA was crosslinked to the filters using a UV Stratalinker 2400 unit (Stratagene) in the auto crosslink mode. Cell debris was removed by placing the filters in a container with a solution of 3 X SSC (20 X SSC contains, per liter, 173.5 g NaCl, 88.2 g sodium citrate, pH adjusted to 7.0 with 10 N NaOH), 0.1% SDS and rubbing the lysed colonies with a Kimwipe. The filters were then incubated at least 3 hr with the same wash solution for at least 3 hr at 65°C. The plasmid library was treated similarly except cells were spread onto a 137 mm circular Duralon UV mem-

For hybridizations, a probe consisting of a 650-base pair (bp) polymerase chain (PCR) fragment representing a portion of a S. cellulosum polyketide synthase gene was used. The fragment

brane placed on top of a 150 mm petri dish containing 80 ml ${\tt LB}$

was amplified using primers to consensus regions of Type I (macrolide) polyketide synthase (PKS) genes (Swan et al., Mol. Gen. Genetics 242, 358-362 [1994]). A series of sense and antisense oligonucleotides were prepared for PCR studies as indicated in the following table 2

5 cated in the following table 2:

Table 2

Oligo-	I. DNA sequence (5'→ 3')	Corresponding
nucleotide		amino acid
		sequence
120 (sense)	CGGT (C/G) AAGTC (C/G) AACATCGG	KSNIGHT
121 (anti- sense)	GC (A/G) ATCTC (A/G) CCCTGCGA (A/G) TG	HSQGEIA
122 (sense)	GT (C/G) GACAC (C/G) GC (C/G) TGCTC (C/G)	VDTACSS
123 (sense)	GG (C/G) AC (C/G) AACGC (C/G) CACGT (C/G) A T	GTNAHVI
124 (anti- sense)	CCCTG (C/G) CC (C/G) GGGAA (C/G) ACGAA	FVFPGQG

The selection of C or G where necessary in the third position of a codon reflects the very high overall G + C content of S. cellulosum (ca. 70%). Conditions for PCR were as follows: 0.01 M Tris-HCl (pH 9.0), 0.03 M KCl, 0.003 M MgCl₂, 0.1% Triton X-10C, 200 µM of each primer, 2.5 U Taq DNA polymerase (Promega), 5.0% dimethyl sulfoxide (Sigma), and 0.01 µg of S. cellulosum chromosomal DNA in a 0.35 ml reaction volume. Reactions were

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carried out in a Perkin-Elmer Model 480 Thermocycler (Perkin-Elmer Corporation, Foster City, CA) under the following conditions: 94°C, 1 min; 50°C, 1 min, 72°C, 1.5 min for a total of 30 cycles. Each possible combination of sense and anti-sense primers were tried. A 650-bp and 350-bp fragment was amplified using cligos 120 + 124 and 123 +124, respectively. The sequence of the fragments were determined using the ALFexpress AutoRead kit to fluorescently label the DNA, which was analyzed on an ALFexpress sequencing apparatus (Pharmacia). The data indicated both PCR fragments possessed significant homology to polyketide synthase genes of Type I antibiotics. The 650-bp fragment was chosen for hybridization experiments.

The fragment was labeled with 32P-dCTP using the NEBlot kit (New England Biolabs, Beverly, MA) and purified on a Bio-Spin 6 column (BioRad, Hercules, CA.). Duplicate blots were prehybridized in 3 X SSC (1 X SSC contains 0.15 M sodium chloride and 0.015 M sodium citrate, pH 7.0), 4 X Denhardt's solution (100 X is 2% Ficoll [Type 400], 2% polyvinylpyrrolidone, and 2% bovine serum albumin [Fraction V]), and 100 $\mu g/ml$ sheared, denatured salmon sperm DNA; all reagents purchased from Sigma Chemicals, St. Louis. The labeled DNA was heated in a boiling water bath for 5 min to denature the strands, cooled on ice, and added to the pre-hybridization solution. The filters were incubated for at least 18 hr in a roller bottle hybridization oven. They were transferred to new bottle, then washed two times in 2 X SSC, 0.1% SDS at 70°C for 30 min (moderate stringency). The membranes were placed on Whatman 3MM paper to remove excess liquid, covered with Saran Wrap, and exposed to autoradiography film (Kodak X-OMAT LS) with two intensifying

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screens. The cassette was placed at $-70\,^{\circ}\text{C}$ and developed at appropriate intervals.

Approximately 100 colonies were seen to have hybridized on the duplicate filters. Fourteen of these were isolated from the master plate and grown in 4 ml LB + kanamycin medium for 20-24 hr, 37°C, 250 rpm. Plasmid DNA was prepared using the standard alkaline lysis method and digested with restriction endonuclease PstI. The digested DNA was electrophoresed on a 0.8% agarose gel in TAE for 3 hr at 100 V. Fragments were transferred to Duralon UV using the VacuGene XL vacuum blotting unit (Pharmacia) and the recommended alkaline denaturation protocol. Hybridization with radioactively-labeled PCR fragment and washing were carried out as described above. Two prominent types of cosmids were observed; one contained PstI fragments of ca. 7.0, 5.0, and 1.1 kb (pEPOcoss and pEPOcos7) that hybridized to the probe; the other type had fragments of ca. 6.0 and 3.6 kb (pEPOcos8 and pEPOcos13) which were homologous to the probe. Restriction analysis confirmed that cosmids showing identical hybridization patterns had identical or overlapping inserts. PCR reactions using primers representing consensus sequences of Type I PKS genes were performed using the isolated cosmid DNA as template under conditions described above, except ca. 0.01 μg of cosmid DNA was included as template. Cosmids pEPOcos6 and pEPOcos8 amplified the 650-bp fragment seen when oligonucleotides 120 + 124 were used, while pEPOcos8 and pEPOcos13 supported amplification of an 1100-bp PCR fragment with oligos 122 and 124. The latter fragment was sequenced and confirmed to possess strong similarity to Type I PKS genes. These data confirm that the recombinant cosmids are related to each other and that all contain PKS-like genes.

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2. Colony blot hybridizations of plasmid library in pZero2.1:

A 137-mm circle of Duralon UV membrane was placed on top of a 150-mm containing 75 ml LB agar + kanamycin. An aliquot of the plasmid library (representing ca. 2,000 recombinant colonies) in 0.5 ml LB medium was spread on the filter. The plate was incubated at 37°C for 20 hr. Colonies were replicated onto two fresh filters which were placed onto LB + kanamycin agar medium and incubated at 37°C for 6 hr. The filters were processed for hybridization as described in Section C.1. Out of 8 positive colonies detected, one contained a plasmid with a DNA region not encoded by either pEPOcos6 or pEPOcos8. This plasmid, called Sau4, was characterized in more detail.

15 3. Colony blot hybridizations of cosmid library in SuperCos:

The recombinant E. coli clones from the microtiter plates (see section 4. b) were used to produce two identical sets of hybridization filters in order to identify cosmids carrying PKS and PS genes. The recomminant clones were spotted onto 2 sets of 22 x 22 cm LB agar plates containing 50 $\mu g/ml$ kanamycin. Each plate contained 384 clones therefore representing 4 microtiter plates. The clones were incubated at 30°C overnight. After pre-cooling for approximately 3 h at 4°C, 20 x 20 cm Hybond N^{\star} Nylon membranes (Amersham, Braunschweig, Germany) were placed onto the agar surfaces. After 2 min. the membranes were removed and placed for 15 min. on Whatman 3 MM paper (Whatman paper Ltd., Maidstone, England) soaked with denaturation solution (0.5 N NaOH, 1,5 M NaCl) before they were transfered onto Whatman 3 MM paper saturated with neutralization solution (1 M Tris-HCl, pH 7.5, 1.5 M NaCl). Subsequently the membranes were

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placed onto Whatman 3 MM paper soaked with 2 X SSC (0.3 M NaCl, 0.03 M sodium citrate, pH 7.2) for 10 min. The membranes were baked for 40 min at 85°C. Then, each membrane was overlayed with 5 ml Proteinase K solution (2 mg/ml Proteinase K in 2 x SSC) and incubated at 37 °C for 90 min. Finally, cell debris was removed by wiping the membranes with a Kimwipe pre-wetted with 2 X SSC.

As we were seeking in particular to identify biosynthetic pathways containing both PKS and PS genes, the following hybridization strategy was taken: The screening was initially focused on ketosynthase domains from type I PKSs and on the adenylation domain from PSs. Target-specific primers were used to amplify DNA fragments of the corresponding genes from chromosomal DNA of S. cellulosum by PCR. The fragments obtained were then cloned, sequenced and the deduced amino acid sequence compared to known ketosynthase and adenylation domains of PKS and PS, respectively. In a second step these PCR fragments were used as gene probes to detect recombinant cosmids of the S. cellulosum cosmid library.

Oligonucleotides based on conserved amino acid sequences of ketosynthase domains from various type I PKS were optimized for myxobacterial DNA by comparison to a known myxobacterial biosynthetic gene cluster (Schupp et al., J. Bacteriol. 177, 3673-3679 [1995]) resulting in primer

25 KS1Up (5'C/A;GIGA(A/G)GCI(A/C/T)(A/T)I(C/G)(C/A)IATGGA(C/T)CCICA(A/G)CAI
(A/C)G-3') and
KSE1 (5'-GG(A/G)TCICCIA(A/G)I(G/C)(T/A)IGTICCIGTICC(A/G)TG-3').
PCR-primers TGD (5'-

T(A/T) (C/T) CGIACIGGIGA (C/T) (C/T) (G/T) IG(G/T) ICG-3⁻¹) and

LGG (5'-

 $A(A/T) IGA(A/G) (G/T) (G/C) ICCICCI (A/G) (A/G) (G/C) I (A/C) (A/G) AA (A/G) AA-3^)$

directed to genes encoding adenylation modules have been described by Turgay et al. (Pept. Res. 7, 238-241 [1994]). PCR reaction mixtures with a final volume of 25 μl contained 0.1 μg template DNA, 0.2 U Taq DNA-polymerase (Gibco BRL, Eggenstein, Germany), 5 μ mol dNTP, 5% dimethyl sulfoxide (Sigma), 1.5 mM $MgCl_2$, 25 pmol of each primer and the appropriate reaction buffer supplied by Gibco BRL. Chromosomal DNA of S. cellulosum was used as template. Additionally, chromosomal DNA of Myxococcus fulvus was used with PS primers. Reactions were carried out in an Eppendorf Mastercyler Gradient (Eppendorf, Germany) using the following conditions: denaturation 30 s at 97°C, annealing 30 s at 55°C, extension 60 s at 72°C for a total of 30 cycles. The formation of ca. 700 bp fragments using the KS primers and of ca. 350 bp fragments with the PS primers were confirmed by 0.8% agarose gel electrophoresis. Fragments of independent PCR reactions were ligated into vector pCR2.1TOPO using the TOPO TA Cloning kit (Invitrogen, Leek, The Netherlands) according to the manufacturer's protocol and transformed into E. coli XL1-Blue. Sequencing of the resulting plasmids and analysis of the deduced amino acid sequence revealed three different KS fragments, designated pM008.4, pM008.6, pM008.7, one PS fragment (pAPs1) corresponding to S. cellulosum and one PS fragment (pDPs1) obtained with chromosomal DNA of M. fulvus. The PCR fragments were re-isolated by digestion with EcoRI from the

plasmids pM008.4, pM008.6, and pM008.7, labeled, pooled and used as gene probes in hybridization experiments as described

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below. The same procedure was performed with the PS fragments of pAPs1 and pDPs1.

Hybridization with PKS and PS specific DNA probes (see above) was carried out using the DIG nonradioactive labeling and detection kit (Boehringer Mannheim, Germany) and performed according to the supplier's manual using buffer containing 50% formamide. The membranes were hybridized in plastic bags containing approx. 10 ml of hybridization solution at 39°C overnight. Unspecific binding of probes was removed by 2 wash steps with 2 x SSC, 0.1% SDS at room temperature for 20 min. and one stringent wash step with 0.5 x SSC, 0.1% SDS at 60°C for 20 min. Detection of hybridizing DNA fragments was performed with the above mentioned system according to the manufacturer's protocol using CSPD as chemiluminescent substrate. The signals were recorded by exposure of the treated membrane to Hyperfilm ECL (Amersham Life Science, Little Chalfont, England) which was developed in appropriate time intervals.

71 signals were detected with the PKS specific gene probe. On the duplicate filters 35 signals were obtained with the PS specific gene probe of which 7 were already known from the PKS hybridization experiment. These recombinant cosmids harbored PKS- and PS-encoding genes. In order to corroborate these results PCR experiments were performed with DNA of the 7 recombinant cosmids as template and PKS (KS1Up, KSD1) and PS specific primers (TGD, LGG) generating fragments of the expected size of approx. 700 bp and 350 bp, respectively (primers and reaction conditions see above).

A comparison of the restriction fragment patterns of the DNA from the 7 recombinant cosmids carrying PKS and PS genes digested by BamHI facilitated an arrangement of the cosmids in

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3 groups. They were represented by cosmids designated A2 and A5. The remaining group was represented by pEPOcos6. Therefore, A2 and A5 represented gccd candidates for further DNA sequence analysis because they carry both PKS and PS genes.

D. Random "shotgun" sequencing of recombinant cosmids and plasmids

1. Library construction

a. pEPOcos6, pEPOcos8, A5, and Sau4: pEPOcos6 and pEPOcos7 were sequenced to completion, and contiguous sequence data and analysis for these overlapping cosmids is presented below for the "cos6 region" (cf. claims 7 and 9). Sequencing of cosmid A5, pEPOcos8 and plasmid Sau4 was taken to the point of large contiguous sequences (contigs) representing the S. cellulosum insert; sequence and analysis presented below (cf. claims 10 to 15).

Randomly sheared libraries were constructed for cosmids and plasmids of interest using a protocol similar to that of of Fleischmann et al., 1995 (Science 269, 496) and modified in Fraser et al., 1995 (Science 370, 397). Briefly, Qiagen-column purified cosmid DNA (~10 μ g) was sheared to a size of approximately 2 kb and the DNA end-repaired using BAL31 nuclease. The DNA was gel-purified after electrophoresis through a 0.75% low-melting temperature agarose gel containing 0.5 μ g/ml ethidium bromide in 1X TAE buffer run at 80 V for 2 hours. The volume of the low-melt agarose gel slice was estimated by adding the gel slice to a microfuge tube and weighing, then 0.1 vol. of 3 M sodium acetate (pH 7) was added and the agarose incubated at 60°C. The temperature was equilibrated to 37°C, and DNA ex-

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tracted twice using an equal volume of buffered phenol (Life Technologies). The aqueous phase was transferred and extracted once with an equal volume of chloroform, then ethanol precipated by the addition of 2 vol. cold 100% ethanol. DNA was concentrated by spinning at 16,000 x g in a microcentrifuge. The DNA pellet was washed with 1 ml 70% ethanol and resuspended in 100 μ l of 0.1X TE. The DNA was ligated to SmaI-digested, phosphatase-treated pUC18 vector (Pharmacia), and single insert recombinants isolated by gel-purification of the band containing vector plus a single insert, followed by T4 polymerase polishing, and a final intramolecular ligation of the vector-plussingle-insert DNA. This final ligation represents a library of highly random ca. 2 kb fragments that was used for shotgun sequencing of the ca. 40 kb cosmids or ca. 10 kb plasmids.

b. Cosmid A2: Cosmid DNA with inserts of *S. cellulosum* was isolated by an alkaline lysis procedure and purified with Macherey Nagel columns (Machery und Nagel GmbH und CoKG, Düren, Germany) using manufacturer's recommendation. Purified Cosmid DNA was sonicated, end-repaired using T4 DNA Polymerase (Boehringer Mannheim, Germany). After gel-purification fragments of a size of approximately 2 kb were ligated into SmaI-digested, phosphatase-treated pTZ18R vector (Pharmacia). The ligation represents a library of highly random ca. 2 kb fragments that was used for shotgun sequencing of the ca. 40 kb cosmid.

2. Sequencing and assembly

a. pEPOcos6, pEPOcos8, Sau4, and A5: DNA (1 μ l of 100 μ l total in the library) was transformed into E. coli by electroporation (20 μ l of Electromax DH10B cells from Life Technolo-

gies) and cells spread onto LB plates containing 50 μ g/ml ampicillin. After growth overnight at 37 °C, transformants (ca. 300-3000 CFU total) were transfered to 96-well growth blocks and shaken overnight at 37°C in 1.3 ml LB medium with 50 μ g/ml ampicillin. Templates were prepared from these cells by an alkaline lysis procedure (Qiagen QiaQuick Turbo Prep) to yield purified, double-stranded plasmid DNA. Cycle-sequencing of the plasmid templates was performed using universal forward and reverse primers and BigDye Terminator sequencing kits (Applied Biosystems), using the manufacturer's recommendations, then resolved using an ABI377 automated sequencer. Sequences were edited using Phred, then assembled into larger contiguous sequences using Phrap (Phil Green, University of Washington, St. Louis, MO).

b. Cosmid A2: DNA (1 μ l of 20 μ l total in the ligation) was transformed into E. coli DH10B by electroporation and cells were spread onto LB agar medium containing 50 mg/ml ampicillin. After growth for 18 hr at 37°C, transformants were transferred to 96-well growth blocks and shaken overnight at 37°C in 1.3 ml 2x YT medium with 50 mg/ml ampicillin. Templates were prepared from these cells by an alkaline lysis procedure (Qiagen Qiaquick Turbo Prep) to yield purified, double-stranded plasmid DNA. Cycle-sequencing of the plasmid templates was performed using universal forward and reverse primers and Big Dye Terminator sequencing kits (PEBiosystems) or Thermo Sequenase fluorescent labelled primer cycle sequencing kit (Amersham Pharmacia Biotech) using the manufacturer's protocols. In the shotgun phase of a cosmid, identical amounts of samples were sequenced either by dye-primer or dye-terminator chemistries (Pharmacia, PE Biosystems). Data were collected using Licor and ABI 377

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automated sequencers and assembled with the GAP4 program (Bonfield, Smith, Staden, Nucl. Acids Res. 23, 4992-4999 [1995]). Gaps were closed using custom made primers (MWG-Biotech) on plasmid templates or PCR products in combination with dyeterminators.

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E. Bioinformatic Methods

1. Open reading frame (ORF) identification

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ORFs were identified in the pEPOcos6 region using the OMIGA 1.1.2 (GCG 0.4D) program from Oxford Molecular Limited. Default values were used (Standard genetic code, all ORFs over 50 bases) to generate ORFs; analysis of these results lead to the list of 14 highest quality ORFs as defined in claim 9. Other ORFs, genes, or genetic elements may be found in the pEPOcos

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ORFs, genes, or genetic elements may be found in the pEPOcos6 insert that have not yet been annotated. In addition to handediting of the OMIGA-generated data, the MAGPIE automated generated personal resistance.

nome analysis tool:

(http://genomes.rockefel.er.edu/magpie/magpie.html)

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was used to identify genes for all the sequenced cosmids and plasmids. ORFs identified in this manner are presented as both nucleotide and peptide files below.

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For cosmids A2 and A5, ORFs have been identified within the DNA sequences of A5 (contigs 10, 11, 12) and of A2 using the FramePlot analysis program from Ishikawa and Hotta (FEMS Microbiol. Lett., 174, 251-253 [1999] public available under [http://www.nih.go.jp/-jun/cgi-bin/frameplot.pl] which is based on positional base preference in codons typical for organisms having genomes with a high G + C content (Bibb et al., Gene 30,

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157-166 [1984]). Default parameters using ATG and GTG as start codons were used. The deduced amino acid sequence of predicted ORFs were compared with protein databases (GenBank, CDS translations, PDB, SwissProt. PIR, PRF) using BLASTP (Altschul et al., Nucleic Acids Res., 25, 3385-3402 [1997]). Additionally, high scoring amino acid sequences were analyzed using the Pfam program [http://www.sanger.ac.uk/Software/Pfam/], which identified specific domain structures of the submitted proteins (Bateman et al. Nucleic Acids Res., 27, 260-262 [1999]).

2. BLAST searches

BLASTP2 similarity searches were performed using the peptide files from the above ORF identification strategy as query sequences. Searches were performed using the in-house Bioinformatics BLASTP2 (Version: BLASTP 2.0a19MP-WashU) web page at the Bristol-Myers Squibb Pharmaceutical Research Institute (allows BlastN2, BlastP2, BlastX2, TblastN, and TBlastX searches). In addition, peptide files generated by the MAGPIE analysis were automatically searched using a FASTA algorithm.

3. Best match and probable identification

Analysis of the BLASTF2 and FASTA output led to an assignment of a best match and probable function. The best match was usually the top scoring match, although sometimes another match was given because it was a more relevant homolog, or no match was found with a significance greater than >e-4. Probable function represents the best estimate of function given the initial analysis of the BLAST data and the published literature regarding the best match, and may not necessarily represent the true function of the gene product (hypothetical proteins are of un-

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known function). A higher probability score indicates a higher liklihood that the probable function corresponds to that of the best match; e.g., the polyketide synthase matches are all above e-100, and given the very high significance scores are presumed to function as polyketide synthases (as are the high scoring peptide synthetases).

The following is a summary of the sequence data from the pEPOcos6 region, pEPOcos8, A5, Sau4 and A2.

10 a. Data from pEPOcos6 region:

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Summary: A large PKS/PS cluster spanning multiple cosmids.

An IS element (designated IS-Sc1 here) is found in the cluster

- this may be a potential tool for genetic analysis of Sorangium.

Statistics: Sequence was assembled from over 2000 random sequences (forward and reverse reads of the ca. 2 kb cloned fragments derived).

47,713 nucleotides of contiguous sequence (no pFD666 vector included)

DNA sequence data are as defined in claim 7.

Note: pEPOcos6_ORF7 sequences (cf. claim 9): the predicted N-terminus of ORF7 shows 145 nucleotide overlap with ORF6.

Note: pEPOcos6_ORF8 sequences (cf. claim 9): >pEPO-30 cos6_ORF8.seq ("ORF9_up" in Fig.2)

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10 57.3% G+C

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Table 3 shows ORF data summary. Note: pEPOcos6_ORF1.seq is truncated at its 5' end; correspondingly pEPOcos6_ORF1.pep is truncated at its N-terminus.

b. Data from pEPOcos8 region:

20 Summary: Two PKS genes found on a cosmid. A Th1000 insertion is also found (occurred during E. coli propagation). No peptide synthetase genes were found; one P450 hydroxylase was identified.

15 Statistics: 1952 random sequence reads from the pEPOcos8 library were assembled using phrap, with 1024 of the sequences assembling into 57 contigs. 12 of these contigs were chosen (totaling 56,537 bp) which each contained >6 reads and consisted of about 1000 bp or more. The sequences of these 12 contigs and the associated ORFs are given below.

DNA sequence data from contigs are as definded in claim 10. Table 4 shows more data.

pEPOcos8 protein data are as defined in claim 11, i.e. for selected ORFs (polyketide synthase, peptide synthetases, or ORFs with high similarity to known genes).

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c. Data from cosmid A5 insert:

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Summary: A cluster of PKS and PS genes found on the cosmid. Other genes possibly involved in this secondary metabolite production include a downstream lipoxygenase gene highly similar to eukaryotic orthologs.

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Statistics: 880 random sequence reads from the A5 library were assembled using phrap, with 530 of the sequences assembling into 12 contigs. 3 of these contigs were chosen (totaling 41,556 bp) which each contained >100 reads and consisted of about 9000 bp or more. The sequences of these 3 contigs and the associated ORFs are given below.

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DNA sequence data from contigs are as defined in claim 12. Table 5 shows more data.

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Protein sequence data from selected A5 ORFs are as defined in claim 13.

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d. Data from plasmid Sau4 insert:

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Summary: Insert contains PKS genes on two large contigs - most similar to the soraphen PKS gene from Sorangium.

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Statistics: 565 random sequence reads from the Sau4 library were assembled using phrap, with 84 of the sequences assembling into 18 contigs. 2 of these contigs were chosen (totaling 6596 bp) which each contained >10 reads and consisted of

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about 1000 bp or more. The sequences of these 2 contigs and the associated ORFs are given below.

DNA sequence data from plasmid Sau4 contigs are as defined in claim 14. Table 6 shows more data.

Protein sequence data from selected plasmid Sau4 ORFs are as defined in claim 15.

10 e. Data from cosmid A2

Table 7 shows ORF data summary

F. Construction of suitable recombinant expression vectors

1. Expression in Myxobacteria

Heterologous expression of the ORFs shown in Figure 1 is performed by using a derivative of plasmid pSUP102 (Simon, R., Priefer, U., Pühler, A., Methods in Enzymology (1986), vol.

118, pp. 643-659). In this plasmid the gene for chloramphenicol resistance is changed for a cassette comprising the gene for streptomycin resistance and the promoter element of the Tn5 transposon. Short homologous genomic DNA segments from the host organism are ligated with the DNA sequences of Figure 1 and with efficient regulatory elements into, for example, the EcoRI restriction site of the vector. Following amplification of the vectors in Escherichia coli the DNA is transfered by electroporation of the host cells or by conjugation with Escherichia coli S17-I (Simon, R., Priefer, U., Pühler, A., Biotechnology

30 (1983), vol. 1, pp. 784-791).

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By means of the tetracycline or streptomycin resistance, respectively, mediated by the vector the host cells are checked for integration of recombinant plasmid DNA into the chromosome by homologous recombination.

2. Expression in Streptomyces cells

Heterologous expression of the ORFs shown in Figure 1 is performed by using bifunctional Strepomyces-Escherichia coli cosmids pKU206 and pOJ466.

3. Expression in Escherichia coli cells

Heterologous expression of the ORFs shown in Figure 1 is performed by using "bacterial artificial chromosomes", cosmids (for example Supercos, Stratagene GmbH, Heidelberg) and T7 expression systems (Stratagene GmbH, Heidelberg; New England Biolabs Schwalbach, FRG). Expression of recombinant enzymes occurs in Escherichia coli cells constitutively expressing phosphopantetheinyl transferase required for the formation of holoenzyme polyketide synthetases and polypeptide synthetases.

Table 3. pEPOcos6 region gene annotation summary (continued).

BEST MATCH (SCORE) PROBABLE IDENTIFICATION	ACOA_BACSU [e-22] acyl-CoA dehydrogenase	AF047828 (e-94) peptide synthetase	U57065 2maR (e-29) antibiotic resistance gene	(no match) hypothetical protein	PKSK_BACSU [e-190] polyketide synthase	283857 ppsE (e-111) polyketide synthase	(no match) hypothetical protein	Y4HP_NHISN (e-20) hypothetical protein	Y4HO_NHISH (e-13) hypothetical protein	Y4RG_RHISH [0-13] hypothetical protein	PKSL_BACSU [e-2] polyketide synthaso	pir(S73015 [e-160] polyketide synthase	AF047828 [e-111] peptide synthetase	AF091251 (0-167) polyketide synthase	AF040570 (e-223) polyketide synthase	AF091251 [e-119] polyketide synthase	(no match) hypothetical protein
MW (DA) BE	26218 AC	. 56317 AF	39092 U5	24819 (n	283282 PK	80545 28	82007 (n	61320 Y4	13102 Y4	11079 Y4	29633 PK	279286 pt	97101 AF	165084 AF	267116 AF	71258 AF	14590 (n
BAA	244	515	352	213	2619	142	758	557	118	103	123	2539	881	1544	2475	1843	140
	1 * 731 732 b 244	1545	1058	639	7854	2226	2274	1671	354	309	108	1617	2643	4632	7425	5529	450
3' # BP	131	2275	3356	4050	4248 12101	14322	16451	14196	16154	16507	17630	25244	27877	32498	32498 39922	45559	46018
'n		ננו	2301	3412	4248	12097 14322	14178 ^è 16451	15866	16507	16815	16830 17630	17628 25244	25235 27877	27867 32498	32498	40031 45559	45599
CENE	ØRF1	ORE2	ORF3	ORF4	ORFS	ORF6	ORF7	ORF7.14 15866 14196	ORF7.24 16507 16154	ORF7.34 16815 16507	ONFB	ORF9	ORFIO	ORF11	ORF12	ORF13	ORE13.1 45599 46018

* The predicted ORF1 gene and gene product is truncated due to cloning of the DNA into the cosmid vector.

b 731 is the last nucleotide of the last amino-acid-encoding codon; 732-735

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11 bp terminal inverted repeat) that is similar to IS1131 from Agrobacterium tumefaciens (IS-66 like d note: ORFs on opposite strand - make up a transposable element from bp 16863-14130 (2733 bp, element, 2773 bp, 4 ORFs, 11 bp inverted repeat)

c note: the predicted N-terminus of ORF7 shows 145 nucleotide overlap with ORF6

is TGA (termination codon). Termination codons have been excluded in the present

annotation.

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Table 4. pEPOcos8 assembly analysis summary (continued).

a. pgPOcos8 ascemblics

ASSEMBLY SIZE (BP)

Contig43 Contig44 Contig49

Contig50 Contig51

pBPOcoa8
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5
and
56
Contig
from
ORPs
selected

qene	5,	'n	d pb	P.A	5' 3' # bp ha best match [score] , probable identificatio	probable identification
Cont 1956_003	3	8675	8673	2890	8675 8673 2890 ERYZ_SACER (e-300+)	polyketide synthase
Contig56_027	10784	8682	2103	700	2103 700 piril60218 (e-300+)	transposon Tn1000 (E. coll)
Contig57_001	92	1210	1119	1119 372		
Cont1957 002	222	222 7001 6780	6760	2259		ALO21899 pks12 (e-267) polyketide synthase (M. tuberculosis)

10														38					
10																			
15		oxygenase									(dans)								
20		Cytochrome P450 monooxygenase									unknown ORF (9. lividans)								
25		Cytochro									unknown								
30		CPKK_SACER [e-50]							•		AF072709 [e-42]								
		CPKK_SP									AF07270								
35	149	419	245	222	411	374	200	155	134	327	492	570	234	308	278	164	134	345	229
	450	1260	738	699	1236	1125	198	468	405	984	12998 1479	12018 1713	70S	927	037	495	405	15715 1038	9
40	6975	8375	9337	9080	1996	.8600	9755	10618	11091	10904	12998	12018	13797	13136	13535	14394	14440	15715	15900
	7424	7116	9074	8412	8432	9724	10621	11085	10687	11887	11520	13730	13093	14064	14371	13900	14036	14678	15211
	Cont.1957_026	Cont.1957_027	Contig57_030	Contig57_031	Cont1957_032	Cont1957_033	Cont1957_037	Cont1957_019	Cont1957_040	Contig57_041	Cont 1957_043	Cont1957_044	Contig57_047	Cont1957_048	Contig57_049	Cont1957_051	Cant1957_052	Cont1957_053	Cont1957_056
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Table: 5. AS assembly analysis summary (continued) a. pEPOcos8 assemblies

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						cantent	best match	probable	
contig	do	ORF	ú	'n	ф	pos.3	[score]	function	identified domains using Plam
2	9435	-	2861	282	2280	% 9.88	AAC44128 (e-170)	peptide synthalase [Saframydn]	AMP-binding as 68-612; pp-binding as 631-697
		7	3525	2902	624	87.0 %	no metch		
		•	6420	4195	2226	95.1 %	P38370 [3e-04]	OmpA fike	
		4	134	7135	99	98.0 %	P39760 [Ze-21]	unknown	
		¥7	7, 36	1950	>1495	96.2 %	no match		
=	18033	-	3636	18%	1778	97.1%	CAB36516 le-134]	peptide synthetase	AMP-binding as 118-520;
:	3	. ~	3588	2501	1086	94.5%	CAB38516 [e-12]	peptide synthetase	DUF4 (domain of unknown function, found
		•							to the carboxy side of pp-pinding sites) as 5-360:
		•	9.65	07.50	653	77 B %	553000 (0-100)	nentific swithelass	no-binding as 1-30; OUF4 as 51-442;
		,	2 7 2	3	1	?		(Pyoverdine)	conflict, ca. 20 as at N-terminus are
									missing (conserved serine residue)
		4	6261	198	2649	64.4 %!	CAA11039[7 c- 65]	potyketide synthase	conflicti
		v	A087	8228	1830	8 976	CAB05094 [e-144]	polytelide synthase	ketoacyf-synthasa aa 14-439;
		,	}		}		•	(Phenolpthiocard	
		4	177.0	Ango.	4234	20 B &	AAD04757 [0-180]	pentide synthetase	AMP-binding as 371-758; pp-binding as
		•	}	}				[Uchamysin]	840-904; DUF4 as 937-1319; AMP-
									binding as 1438-1825; po-binding sa
									[1907-1071; DUF4 aa 1969-2388; AMP-
									binding as 2485-2889, pp-binding as 2072, 1006
								peptide synthetase	DUF4 29 45-476;
12	15898	-	-	1545	>1545	97.5 %	AAC68816 [49-74]	(FK506)	
								cytochrome P450	
		7	2883	<u>5</u>	1335	2.4.2 2.4.2	P43492 [0-07]	enzyma	
		60	4659	2911	1749	92.5 %	NP 001130 [5e-56]	iponygenasa	
		4	2836	7066	1191	95.2 %	no match		
		ß	208	7822	621	90.1%	no match		
		9	8974	7943	10 2	87.8 %	no match		
		. 7	12001	11252	750	92.6 %	no match	_	
		•	13533	12181	<u>35</u>	90.3 %	no malch	:	
		6	15897	13961	1917	80.9 %	CAA19149 (e-08)	regulator	

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b. selected ORFs from cosmid A5

32	,	-	F Up Bad	000	dest match score probable identification
Cont1910_001	2861	582	2280 759	159	U24657 saframycin (e-155) polyketide synthase
Contiglo_006	2880	3323	444	143	
Cont1910_007	3876	2902	975	324	
Cont1910_000	2953	3957	1005	334	
Contig10_009	1357	3299	1059	352	
Cont1910_013	4180	6585	2406	601	
Contiglo 016	7033	2600	1434	111	
Contiglo_017	7043	6138	906	301	
Contig10_010	6500	7219	720	239	
Contig10_019	6954	7295	342	113	
Cont1910_020	6982	797	916	172	
Cont1910_021	7819	7040	780	259	
Contiglo_023	7415	8029	615	204	
Contig10_024	7794	9435	1642	548	
Contiglo_027	9435	9008	630	209	
Contlg11_001	011	417	354	117	
Contigll_002	2526	751	1776	165	AL015640 (e-113) peptide synthetaso
Cont1911_004	1033	2787	1755	594	
Contig11_005	3500	1977	1524	507	
Contig11_007	3586	2501	1086	361	
Contigl1_008	2507	3814	1300	435	
Contioll 011	5213	2570	1636		

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10														ENASE													
15	polyketide synthase			de synthase	synthetase			synthetase						Arachidonate 5-lipoxygenase													
20	polyketic			polyketi	+) peptide			s) peptide						ARACHIDON													
25	rifamycin			uberc [e-129]	mycin (e-300			Streptomyce						=													
30	AJ223012 [e-52] rifamycin			283857 ppsE M. tuberc [e-129] polyketide synthase	AF047828 syringomycin (e-300+) peptide synthetase			AF082100 (e-63) (Streptomyces) peptide synthetase			•			LOXS_MOUSE (e-54)	٠		•										
35	882	433	394	1213	3079	210	108	514	456	250	318	444	. 1049	285	180	191	192	171	202	396	398	458	179	242	225	230	544
	2649	1302	1185	3642	9240	633	327	1545	1368	1653	957	1335	3150	1749	543	594	519	916	609	1191	1197	דרנו	240	729	678	693	1635
40	3811	5210	6735	6229	17329 8090	16733 17365	T35 1772 18571	1545	~	1655	1361	1549	4926	2911	2065	5231	5520	5541	6373	7086	5839	1331	7010	7822	7318	1716	9550
40	6429	6511	5551	6686	17329	16733	17397		1369	M	2317	2883	1111	4659	4523	4638	4942	9609	\$765	9689	7095	5955	1549	7094	7995	6408	7916
45	Contig11_012	Cont1911_016	Cont1911_018	Contig11_021	Contig11_026	Contig11_048	Cont 1911_049	Cont1912_001	Contigla_002	Cont1g12_003	Contig12_005	Contigl2_006	Contigl2_007	Contig12_009	Cont1912_011	Contig12_012	Cont1912_013	Contig12_014	Contigl2_015	Contiglz_016	Contigl2_017	Contig12_018	Cont1912_020	Contig12_021	Contigl2_022	Cont1912_023	Cont1912_024

310 674

12184 11252 933

Contig12_033 Contig12_035

Contig12_036 Contig12_039

Contig12_029 Contig12_030

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Table 6. Saud assembly analysis summary.

a. plasmid Sau4 assemblies

Assembly size(bp)
Contig17 2581
Contig18 4015

b. selected ONFs from cosmid A5

dene	.s.	5	pb.	Paa	best a	atch (scor	el prob	1' bp laa best match [score] probable identification
Cont1917_001	2485	_	2485	629	U24241	2485 1 2485 629 U24241 Sorangium [0-213]	[6-213]	polyketide synthase
Cont1918_002	2	1510	1509	205	U24241	2 1510 1509 502 U24241 Soranglum [e-105]	(e-105)	polyketide synthase
Contig18_010	1494	4015	2522	841	U24241	1494 4015 2522 841 U24241 Sorangium (e-245)	(e-245)	polyketide synthase

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Table: 7. ORF data summary from A2 insert

		identified domains using Pfam	pkinase aa 47-294:	,		acyl-tRNA synthelase (IRNA-synthase aa 27-694;	oxidoreductase FAD/NAD-binding domain	aa 110-227;	aminotran_1 aa 2-385;	L-dopa decarboxy/ase pyridoxal deC as 48-411	short chain dehydrogenase domain sa 53- 240;	keloacytsynthase aa 13-438; acyt transfase aa 533-854; short chain	dehydrogenase domain aa 1159-1357; pp binding aa 1451-1515;	OUF4 as 17-409; AMP-binding as 507.	sus; pp-dinong as 991-1054; DUF4 as 1067-1466; DUF4 as 1544-1844; AMP. bloding as 2041-2439; pp-bloding as	2525-2589;			Sigma70 ECF aa 17-83;			HTH aa 5 11-109;	response reg aa 46-159; signal aa 326-	542; respanse reg aa 590-703;
	probable	function	regulation	[serine/threoning	Separa vision	acyl-tRNA synthetase	monooxygenase		aminotransferase	L-dopa decarboxylase	oxidorecucinse	polyketide synthase			ay me case		peptidase		sigma factor		regulation	regulation	regluation	
	best match	[score]	P54744 [5e-37]		no match	CAA15124 (>e-180)	AAC32457 (2e-17)	•	CAB42045 [9e-67]	AAD21754 [8-113]	CAB41201[7e-41]	CAB06094 [<e-180]< td=""><td></td><td>AAC80285 (<e-180)< td=""><td></td><td></td><td>BAA13079 [2e-44]</td><td>no match</td><td>CAB09733 [2e-63]</td><td>no match</td><td>CAA19900 [e-37]</td><td>CAA19859 [3e-15]</td><td>BAA17885 [26-50]</td><td></td></e-180)<></td></e-180]<>		AAC80285 (<e-180)< td=""><td></td><td></td><td>BAA13079 [2e-44]</td><td>no match</td><td>CAB09733 [2e-63]</td><td>no match</td><td>CAA19900 [e-37]</td><td>CAA19859 [3e-15]</td><td>BAA17885 [26-50]</td><td></td></e-180)<>			BAA13079 [2e-44]	no match	CAB09733 [2e-63]	no match	CAA19900 [e-37]	CAA19859 [3e-15]	BAA17885 [26-50]	
2+ S	content	pos.3	94.4%		80.7 %	96.0 %	94.7 %		74.4 %	85.5 %	%99	87.6 %		88.0 %			% 9·98	98.9 %	95.3 %	95.7 %	94.2 %	_	86.8 %	
		ф	>1666		1734	2703	738		1158	1539	945	1 81		7887			1020	1320	951	486	417	357	>2127	
		3,	7		3338	3398	6374		. 8433	9855	12712	19984		27889			29402	30401	32932	33613	34077	35255	35730	
		'n	1666		1605	9100	7111		9290	11393	13656	15374		20003			28251	31720	31982	33128	33661	35611	37856	
		ORF	-		7	C	4		S	9	~	6		o,			2	=	12	£	7.	5	92	

Claims

Claims

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	1. DNA sequence, the expression products of which cause an
	enzymatic biosynthesis, a mutasynthesis or a partial synthesis
	of polyketide or heteropolyketide compounds or are involved
15	therein.

- 2. DNA sequence according to claim 1, wherein the polyketide or heteropolyketide compounds are epothilones.
- DNA sequence according to any of the preceding claims,
 wherein the DNA is derived from myxobacteria.
- 254. DNA sequence according to any of the preceding claims,15 wherein the DNA is derived from Sorangium strains.
- 5. DNA sequence according to any of the preceding claims, wherein the DNA is derived from Sorangium cellulosum.
- 20 6. DNA sequence according to any of the preceding claims, 35 wherein the DNA is selected from the group consisting of:
 - (a) the following DNA sequence:
- 40 25 Seq ID No 1 (A2 cosmid)

GGATCGCGGCGCCCTCGCGCTGCTCCTCGAGCGTGCGGAGGAACTCCCACGCCAGGCGCGACT

TGCCGAGGCCAGGCGCCCCACCACCACCACCGCGTTCGCGGAGGGCTCGTCGACGCAATGGC
GCCACTCGGTCGCGAGGCTGCGAGAGCTCCCGCCCCACGCAGGGCGTCGGCTTGCCGA

GGAGCCGTGGGACGCATCCGGCTCCTCCTTCGGGCCGCAGCCCCCTCCGGGCCCCCT

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GTACCGTCTCGAAGCGGCTCGCGAGCAGGCTGGCCGTCGTCGAGCCGGATCTCCGGCG GCGACAGGCCATCTCGCCCGGCGATGAGCTGCGCGACCCGATCGACCAGCTCGCCGACCGGCA 10 GCCTCGCCTCGACCTCGGCCAGCCCTGTCGCGACGGCACGGCCACGCCTCCGAGCGCCGCCC GCAGCGCGAGGGCGCAGTGGGCCGCCGTGTGGCGAGATCCGTGGGCGACTCGGCGCCGGACA 15 GCGCGGCCGCGCGCGCCCCGCCCCGATCGAGAGCCCCTCGCCGGCCACGGCGGCGA GCTCCGCCGCGGCGGCGCCGTCGCGCGCCGCTTCTTCGCCAGCATCCGCG 20 $\tt CCACCAGGCGCTCGAGCGGCTCCGGGGATACCGTCGCGGAGCTCCCCGAGCCGCGGCGGCTCTT$ 1.0 GGCACTGGAACAGCACGCACCCGAGCGCGAACACGTCGGCCCGGGCGTCGACCGGCGCGTCGC 25 1.5 CGCCGAGCGTCGTGGCCACGCGCGCCAGCGCCACGCTCTCGGCCAGCGTGAGCGGCGCCC $\tt CGGCGAGCCGCTCCAGGGTCACGCCGTCGAGCCACTCCATGGCCAGGTACGGCCGCCCTG$ 30 $\tt CGCCGGTCACCCCGTGCGCCACGTACTGCACCACGCCGGGCAGCCGGAGCGTCACGAGCGCCT$ CCGCCTCCCGCGCGAACCGGCGCAGGTCGTTGGCGCTCGCGCCCTGCAAGACCTTGAGCGCGA CCGCCTGCCCGGACACCCGGTCGCGCGCGCGGTACACGTCCCCCATCCCGCCGGAGACGGCGA 20 35 GCCGCTCGATCTCGAAACGATCCTCGATCACATCCGCTGCGCGCATGGCGGTGCCAATGTACT CCGCGCGAGCCTCGGGCCCCGCGCGTAAGTGCGGCCCTGCGCCCGGTTGAACGCCAGCCCGA GCGTGACCGCCTCGCGCTCGGGATCCACGGCCGGGATCGGTCCACGCCTCGACGAGCGCCT GCGTTGAACAACCCGCCACCGGGCGCACGCAGCCGGCATCGCCGCGCTGGCCACCCGGCGCTG 40 CCGCCCTTAGGCTCACCTCCGCGATGCCCCGCTGGTTCAACACGGCAGGTCCCTGCAACCCGG CCGATCACTACATGCTCCCGGCCGAGGAGCGCTTGCCCGCAGTGCGCGATCTGGTCGATCGCA AGGCCTACTTCGTCCTGCACGCCCCGCGGCAGATCGGCAAGACGACCTCGCTGCGCACGCTCG 45

TCGGGGCCGCCTGCGCCTGGGCTCAGGCCGCCGCCCGCTCGTCGTCTTCCTCGACG AGGCCGACGCCCTGCGCGACGCGCTCGTCTCCCTATTGCGCCAGATCCGCAGCGGCTATC 10 $\tt CCGACCGCCCGCGTGACTTCCCGCACGCGCTCGCCCTCGTCGGCCTGCGCGACGTGCGCGACT$ ACAAGGTCGCGTCGACAGCGGCAGGCTCGGGACGTCGAGCCCCTTCAACATCAAGGTCG AGTCGCTCACGCTGCGCAACTTCACCCGCGACGAGGTCGCAACACTCTACGCTCAGCACACGG CCGAGACCGGTCAGGTCTTCCGGCCGGACGCCGTGGACCGCGCCTTCGAGCTCACCCAGGGCC15 AACCCATCACGTCTGCGAACGTCGATCGCGCCAAGGAAATCCTCATCGAGCGGCAGGACACAC ACCTCGACAGCCTGGTGGATCGGCTGCGCGAGCCGCGCTCCGCGGGGGTGATCGAGCCGATGC 20 10 TCGTGCGCATGACCGCGGAGGGCGGCCTCGACGTCGCCATCTACCGCGAGATCATCG ${\tt TCCGCGAGCTCGCGTTCCCGATCCGCGCCTCACTCCCCCAGATCAAGGCCACGTGGCTCACGC}$ AGGACGGCCTCGACGCGGACCGCCTGCTCGACGCCTTCCTCCTTCTGGCGCCAGCACG 25 GCGAGCCGCTCCTCGGCGCCCCCTACCATGAGATCGCCCCGCACCTCGTGGTGATGGCCT 15 GGATGGATCTCTGCGTTCGTTACGCGGGCGAGACGCTCGCGATCGAGCTCAAGGTCTGGCGAG 30 GCCTCGATCGCGGATGGCTCATCCTCTTCGACCAGCGCTCCGGACAGCCCCCCCATCGCCGAGC GCACGCGCGCGAGCGCGCCGCCGCCGCCGCCGAGGTCGCCGTCATTCGCGCCTGAG 20 35 GCACCACCAGGACCTCGCCATCCGCGAGCTCCGGCCGCTCCACGAGCGCGTGCGCGCCCGCGC GCACCGCCGTGAGCACGTCTCCCAGCGCCGGCTTCAGCCGCGCCCAGCGTCGCGGCGTTCGCCC 40 CCGCCGCCATCGCCGCCGCCAGATCCAGGAGCCCCGGATCCGAAGGCGCCGCCGACCGCCG $\tt CGAAATCCGCCGCTGAAGGCCACTTCGCCCGGTGGATCGAGGTATCGCCCGTCTCCTCCGCGT$ ACACCCAGCGCCAGACCTCGTCGGTGATGTACGGCAGGACCGGCGCGAACAGCCGCAGCAGCA 45 CGCCGCGCCCCGCGCCTTCGCGAGCTCCAGGTAGGCGTCGGTGAACCAGCGCCAGAAGAAAT CCTCGGTCCGCTCGAGCGCCGCCGCGAACTCGTGCTCGAACGAGCGCGTCGCGTCGTCCA

		CCACGGCCGACAGCTTGTGCAAGAGCGCCCGGTCGAGCTCCTCGGAGATCGGGTGGACCTCCG
10		CCGACTGGCTGAGCACGTACTTGCTCGCGTTCCAGATCTTCGTGACGAGCCGCTTGCCGATCT
		TCAGCACCTTCTCGTCGAACGCCGTGTCCGTGCCGAGCCGCGCGCTCGCCGACCAGTAGCGGA
		CCGCGTCCGAAGAATACGTGTCGAGCAGGTGCATCGGCGTGACGACGTTGCCCTTGCTCTTCG
	5	ACATCTTCTTGCGATCCGGATCGAGGATCCACCCGGAGATCGCGACGTGGTGCCACGGGACCG
15		ACGACTCGTGCAGCATCGCCTTCGCGATCGTGTAGAACGCCCACGTCCTGATGATGTCGTGGG
		CCTGCGGCCGCAGATCGGCCGGGAAGAGCCGCGCGTGGCGCGCGGGATCGTCCCCCCAGTGAG
		AGCTGATCTGCGGCGTCAGCGAGCTCGTGAACCACGTGTCGAAGACGTCGGACTCGGCGGTGA
		AGCCGCCGGGCTGGTCCCGCTGCGACGCCTCGTACCCGGGCGCACGTCGACCGTCGGGTCGA
20	10	CCGGGAGCATCTCGCGCGTCGCGAGCAGCGGCCGGCTGTGATCCGGGTTGCCCTCGGCGTCGA
		GCGGATACCAGACCGGGAACTGCACGCCGAAATACCGCTGGCGGCTGATGCACCAGTCACCCT
	•	GGAGCCCCTCGGTCCAGTTGCGGTACCGGAGGCGCATGAAATCCGGGTGCCACTTGATCTTGT
25		CGCCGTATTCGAGGAGCTCGGCCTTCTTGTCGGCGAGCCGGACGAACCACTGCCGCGTGGGCA
		CGAACTCGAGCGGCTGGTCGCCCCGCTCGTAGAACTTCACCGCGCGCTCGATCGGCCTCGGCT
	15	CGCCCCGCAGCGCCGGCCCGGCCGGCGCGCGCGCGCGCG
		CCACCGCCGCGCGCCTGCTTCACCCCCCTGCCCTGGAGCGCCGCATACGCGGCGTTGGCCG
30		CGGCCGGGTCGCGGCTCTCCCACGCGCCCTCGCCGAACGTCACCGGCAGGACACGGCCGTTCT
		TGCCGAGCATCTGCCGGAGCGGGAGCTTCTGCTCCCGCCACCAGATCACGTCGGTCG
		CGAAGGTACAGACCATCAGGATGCCCGTGCCCTTCTCGCGATCCACGAGCGGGCTCGGGAAGA
35	20	TCGGCACCGGCGCGCGGAAGATCGGGGTGAGCGCCGTCTTGCCGAAGAGGTGCTGATACCGCG
50		GGTCCTCCGGGTGCGCCGTGACGCCGACGCAGCCGCGAGCAGCTCCGGGCGCGTCGTGGCGA
		TGACGAGCTCCTCGGCCGTCCCCTCCACCGCGAACGCGATGTCGTGGAACGCGCCCGATTGCG
		GGCGATCCTCGACCTCCGCCTGGGCGACCGCGGTCTGGAAATCGACGTCCCACATCGTCGGCG
40		CGAAGACCGAGTAGAGGTGGCCCTTCTCGTGGAGATCCAGGAACGACAGCTGCGCCGTCCTGC
	25	GGCAGTGATCGATGGTGGCGTACTCGTTCCGCCAGTCGACCGAGAGGCCCACCCGGCGGA
		AGAGCGCCTTGAAGACCTGCTCGTCCTCGCGCGTGACCTTGTGGCAGAGCTCGATGAAGTTGG
		GCCGCGACACGATGCGCGGCGGCTCCTTCTTGATCGTCTCCGGCGCGGCCTGCGGCAAGGTCA
45		GGCCGCGCTCGTACGGCGTGCGCACGTCGGTGCGCACGTGGAAGTAGTTCTGCACGCGCCGCT
		CGGTGGGCAGGCCGTTGTCGTCCCAGCCCATCGGGTAGAAGATGTTGAAGCCGCGCATCCGGC
	30	GCTGGCGGACGACGTCCGTGTGCGTGTAGCTGAAGACGTGGCCGATGTGCAGCGAGCCCG

 ${\tt GGTACGTCCGTCGGCCTCCCACAGGTCGGCCAGGCCGAGCTCGGCGAGTCGAAGT}$ 10 GCTTCGCGAGCGTCGCGGGATCGATGGAGCGGAACGTCTTCTTGATCGTCACGTGGTCACCTG CAGAACAGACCCCGCAGGAACCGCCCGCGGGGCCGGCATCCTACGTCGTCCCCCGGGTGCCGC TCAAGGCGCGCGCGCGCGCGGCGGCGATCCGCGATCCGCCATCCGCCAGAGCCC 15 GGCGGCTCCGCCGGCGCGCGCGCCGTCCGTGGAGCCGAGAGGAGAGGCCGGCGCCCAGGTC GGCCGGGGGCTCAGTCGTAGCGCTCGACGTGGACGTGCTTGCGGTGGACGCCGAGCTCGCCGC GGGCGAGCTCGCGGACGACGAGACCATCCGATCCAGGCCGCAGATGAAGACGTGCGGCGCCG 20 10 GATCTCCGCTCTTCTCCGCGAGCTCCCGGTAGAGCTCGGGCACGTGCGCCTGCACGTAGCCGC GGCGGCCGGCCGACGGCCGCGCGCGAGAGCGTGATCTCGTAGCGGATCCGGTCGGATC GGATCCACAGGTGGGGCGCGGCCAGCCCCGCGCGCAGGGAGGCGCAGCATGCTCCGGAGCG 25 GCGTGATGCCGGTGCCGGTCGCGACGAACAAGGAGGGCGCGGAATCCCCGGGATCGCGGGTGA 15 $\tt ATGCGATGGAGTAGGCGCGCTTCACCTCGCCGCCCGGGAGCGGGAGGACGAGGTTGACCCACT$ 30 GGCCCGCCTCGAACAGAACGACCTCCCGTCGGCGCGCTCGAACGAGAGCTCGCGCACGAAAG 20 35 GATCCTGGTTGGGGAGCGCGCGCGGGGCGGGGGATCCCGGTGCGCGGGGCTTCTGCGCGGGGA 40 GCTGCCCTCGCTGAGCCGGGCGCTGGTCGGGCGACTTGGCCGAGCCCAGCGCGAGATCGGAGA ${\tt CGGGGAGATGCGCGCGTCGCTGCATAGAATCCTCCATGGAATCGGTCATCAACACATCGGGAA}$ GAGCACCCAGGCTGAAAGAACCTTCGAAGAACCGGCTCTCATACACCCTCCATTCATCGTGC 45 ${\tt GACCCCGGATTCAGGACGGATCGAACCCGCGAGGGACGCTGGCTCTCTGGGCCTCTCCCTGCT}$ CGCTCGACCGGCGCCTCTCGACGCAACTCCGCCGTTCGTCGGGACGGGACGGTCCGCCTCGC

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10 GCTCCGTCCCGCGCGCGCACGACGCGAGCTCGCGCGGGGAACCGCGGGCCGCTGTCGTGGCT GCTGATGCGCGACGATACAGGGGGGACGCCGTGCCTACCTGGGCAACAGGCGCTCATCTTCTA GTGGTGTCAGCGAGAGATGCGCATGGTGGACGCGGGCTACGCGTCGAGAGGGACACTAGCACT 15 CTGGCCGCTCGCCGCTGGCCGCTGGCCGCTGGCCGCTGGCCGCTGGCCA TGTGCGACGTGAGCTCGAGCAGCCCGCGGCTGACGGACAGACCCCGGAGTTCATCGAGCCGGT 20 GATGCCGAACCCGCCAAGCGAAAAAACGTATCCGTTCGGCAGGTCGTGGCCTATCATGCAAGC 10 TGCTCGATGCGCTGACAGGCTTCTTCGAGATCCTCGTCGGTCTTTGCGAAGCAAAACCGCATG AAGCGACTCCCCTGCGTCCCTTCAAAGAAGGCGTCGCCTGGCACGCCGCCACCCCGGTCTCG ${\tt TCGAGCAAGTAGATGGCTCGCTCTCGACCTGTCCTCCCGGGTAGGCGAGACACATCCGCCAGC}$ 25 ACGTAGTACGTCCCCTGCGGCACGCAGGGTGGCAAGCCCGCTTTCTCCAGCGCCCGACAGAAC ATCCCGGCAGCGACTCCATGCTGCAGCGGCGTCGGCGCGCAGACATACAGCAGGTCGCTCATG GCTCCAATGGCCTTCGCCCACCTGGCATCGGCCACGCTGTAGCCGATCCGCCATCCTGTGATG 30 ACGCTGACGTGCTCACGGCCGTCGAAGATAAAGTACTCGTAAATTTCGTCCGTGATCACCATG AGGTCATGGTGGCAGGCGAGATCGGCGGATCTGTTCCAGCTCCATTCGGCCGAACACCTTCCCG 35 ${\tt GAAGGATTTCCAGGAGAGTTCACCACGATCGCCTTTGGTCTTCGGGGTGATCGCGCGCTCCAGC}$ TCGTCGCCGTCGACATTCCAGCTCAGGGATCGCGCCGTCACATACCGCGGAACAGCCTCGACG GCGAGGATAGCCTGGGCGTGATAGGCATAAAACGGCTCGAAGAGCAGCACTTCGTCCCCAGGA TTGAGCAAGGCCATGCAAGTGGCCTGAAAGGCCCCTGTCGCTCCCGGCGCTCACCGTGATGTCA 40 GTCTCCGGATCCGCCGCGATGCCATTATGGCGAGCCAGCTTCGCCGCGATCGCATGGCGCAGC 25 TCCACGATGCCGTCGAAGCGCGAATATGTATTGCACCCCCGATCCATCGCCTCCTTCACCGCT TGAAGGATCACCGAAGGAACTGGGGTATCACAGACGCCCTGGGACATATTGATCCCATGGACC 45 TTGGCGCACGCCAGGGTCATGGTACGGATATCGGACTGGGCGAGGCGAGCCGCACGATCACTC GGTAGACTCTTCATCAGCGTGCTCCTGCTTCTGTTCTGCGGCTCTGCATGGTGTCTTCGGGTG 30

TTCTTTGATGAAAGCGAGACATTCGGCCTTTTCGTGCCCTGTTTGCCCGCAGCCCTCCAGCCCCC ${\tt AGGTACGGGCTTGTCGGCGGGCCAGATCGAGTACTGCTCTTCGCCGTTCACCACGACCTGGCAGGGCAGGCAGGGCGCAGGGCAGGGCAGGGCAGGGCAGGGCAGGGCAGGGCAGGGCAGGGCAGGGCAGGGCAGGGCAGGGCAGGGCAGGGCAGGGCAGGGCAGG$ 10 CATGAAACGAATCGCTCATCGGCGCACAGGCGCGCGCCGGCTGCCCGGAGGCACTCCCACGCC TCCCTCACGGCAACCTCATCGCTCCGGATGTTCCCGATGGCGACTCGGATCGTGACCTGCCG TGGAGACGGGTATGGGACAAAAATACCCTGCCCGACTTGTTGACCTCGTCCAGCAGCGCCTCG 15 TTGAGGCGATCGAGCTCGCTTCGATCGACTCTCTCTCTCGCCTCGCCCGACCGCATGATG CAAGCGAGCGCGGAGGGCCT'CATGCGAAAGCAGACCGTACTGAACGGCGTCGGCGCGAGGCGC TCCCAATCGGGATCGGCGTCCACCCACTGGGCGAGCTGCTGCCCCAATCGGAGGTGCTCCCGG 20 ATCCGGGCCGCCAGCCCTTCATGCCCGAAGTAGCGCACGATCATCCAGAGCTTCAGCGCTCGG 10 AAGCGCCGACCGAGCTGGATACCCCAGTCCATGTAATTCGTGACGTCGCCCTCGGTGCGGAGG CAATCCATGGGGGTGAACAGCCACTTGTGAGGGTTCACTACCAGCGAGTCCGCCCCTCGCAG 25 TGAAGCCATAGCCCGTGCTCCCGGCAAACGCTGACGATGGCGGGGATGGGGTCGACGCTCGTC 15 ${\tt ACGACGGCGCGCGCGCGCCTCGGGGGACCATGCGGAAGGCCGGATCCGTGGGGATCTTCCGC}$ 30 GACGCGTAGAGTCGCATGCCCCGCCTGTCCCGCCATGCCCCGGAGCCGGATGGTCGGCTCGGCC GAGTCGCGCGCGCGCGATCGCGACCATGCTGGCGGTCGACGCGGTGTCCATGATCGCGCCG 35 TGCAAGCCGGCGTCGAGATCCAGCATCTGACGCAGCCAGGAGGAGGACGAGCTCCTCGAGCTCG GTGGCCGCCGGCGACGTGCGCCATAGCATCACGTTGACGTTGAGGCACGCCGCGAGCAGCTCG CCGAGGATCCCAGGACCAGACGCCGTGTTCGCGAAATACGCGAAGAATCGCGGATGATTCCAG TGCGTGATCCCCGGCAGAATGATCTGCTCGAAATCGGTGAGCACGGCGTCCATCGGCTCCGGC 40 TCGACGGGGGGGGGGGCCAGCCTGCCCTTCACGTCGCCGGGGGCGGATCGCGGGAAAGACG GGGTATCGATCCGGGTGGCCGAGGTAATCGGCCGCCCAATCGATGATTCTCATACCGATCCGG CGGAACTCCTCCAGATCCATGTCCCCGAGCCGTTCTTTCCGCGGGTCGCTCACGTCAACCTCC 45 TCGCCCTGCCAGGACAGGATCCTCGAGGTCCCCTGGCTCCGGCGGTGGAAAGCGCTCCTTGAA CGTGAAGGCCCACGGGGTCGGTCCGTAGCGCCGCAGGTGCTCGAGCCGATCCTGCCCCTCGCG ${\tt GACGGACGGCATGTGCCCGGCCGGGACCCACCACCACGAGGTAATGCGGCTCGAGATGCTC}$

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		GAACCACCGAGCGCGCTGTCGCAGGAACGCGGCATGATCCGCGGTGTAGGTGAAGGCGAACAG
10		GTGCTCGATGGAGGTCCATACCGACAGGGTCACGAGGAGCCGCTGGTCCGGGTACGGACGG
		GGACACAGAGTTCCCCTCGGCCGTCTGCAGGCGCCACACGAACCCCTCGCTCCGATCGGCCAG
		ATGGTTGATATGGTCGAGCCCCTGGACGAGCCCTCCATGATCGGATCCTCCAGCGGAGCGCG
	5	AATACATGCGAAGTTGTATTGCGCGATGTGGTGCCGATGTCCGACATGTCGCTTTCCATCTC
15		CAGCTCCCGCTCACCAATCCCAGCGCTGCTCCGGGGAGCTCATCAGGGCAGACGCGACATCGA
		TCCCGAAGCTCCGCCGCATCCCCTCGACGAAGGCGGCCTGGACCGCTTCGGCGACGGATCGGC
		CTGCCTCCGGCAAGACCTCGGAGACAAGAAGAACCGCCTCGTGGAAGGGACAATCTTGCCCC
		GCTCCGCCTGGCGCCATACGAAGTGCCTCGTCACCAGTCCCTCCGCGTCGGCATACCCGACCT
20	10	CGCCGGCGCCGACCCCTGCCGCCTGAGCCGAGCTCCACGAACGCCTCACCGCCTCGCG
		AGATCTCGAGGCGAACGTCCGGGCCAGCCAGATCGCCGAGGTCCCAAGCGCCGACGGGGACGG
		CGAACCGCAGCGACAGGAGGTTGTAAAAATCGACGAATGCGTTGATGTGCGGCAGCTCTCCAC
25		CACCGAGGACCCGCTTCGCCAGCGCCTCGATCGAGCTCGGAAATTTCTTGCCAGAGACCCCCA
		CTCGCTTCATCGCCTCGCGCCAGGCAGCCACGTGCGGATGCGACTGGGCGTTTTCGTGGCCCC
	15	AGCTCCGTCGCAGCTCCTCGACCTTCCGGAGCTCCTCCAGCACGGCCGGC
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30		GCGGATCGACGATGAATGCCATGTGCCTCCTGCCCTCGAGAGCGATCGCCTCGATCGA
		AGGCTGTGGATGCATGAGCCGGGCCGTGCGGACGCAGGACCCCGCTACTCATGGCTCTTCGTG
		GCCGATGAACAGGTCCTCCACCCGTCGATCGTGCTCGGTGCCCCGATCCGTCCAGTCCCACCC
25	20	GCCGGCGACCGCGATGTTTGCACCCGAGACGTACGAGGCGCGGTCGGAGGCGAGGAACGCCAC
35		AGCATCTGCGACCTCGCTGGCGCCCCAGGCGGCCCATGGGGACGCGCCGCTCCATCCA
		CTTCTGCGCGGGCGGAAGGTATCCGTTGTCGATGAGCCCTGGAGACACACAGTTGACCAGGAT
		TCCATGAGGCGCCTCCTCCGTGGCCAGGCTGCGCGTGAGGATGAGCACGCCGGTCTTCGCGAT
40		CGAGTACGCCGCCACGTTCGGCGCGCGCGGATCGCGTACGTGGGGCTCAACCCGATATTGAT
	25	GATCCGGCCGCTCTTTCGCTGGCGCATGCGCGCCACGGCCGCGACAGAGGTAATGAACGCT
•		GCTCAGGTTGCTGTCCATGACGTTGCGCCATTCGTCGTCGTCATCGCCGCAAGCGGCTTGAA
		GAAGAAGTCGCCCACGTTATTGACGAGGATGTCGATGGGGCCCAGCTGCGCCTCGACGCTGGA
45		GAAGAGCTCCGCGGCCGCGTTGGGGCGGGTGACGTCGGCCTGCACCACCATGGTTCGTCGCCC
		GAGCGCGCGGATCTCGGCCGCCGCATCCTTGTTCGAATGGTAATTGACGGC
	3 C	GACGTCCGCGCCTTGCTCCGCGAGGCGCAGCGCGATCGCCTTGCCAATTCCGCGCGAGCTACC

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GGTGACCAGGGCGACGCCCGGCGAGCTCCAGCGATCGCGCCTGTGGCAGGGCCGGAGCAGC $\tt CTCCTGGTGGAGGTCGACGGGGGGGGGGCTCCACGTGGTAGCTCGTCTCTCGCGGAGCCGC$ 10 GCAGTACCTCTCGTAGAACGCCTCGAGGACGGCTCTTCGCGTCGCATGATGTCCGCGTGGGA TTCGGCGCTGCGCCACGGATAGAGCACCAGGATCTCGTCGGGGCGCACGGTGCTCTGAAAGAA ${\tt TCGCGCATGACCGCACCACCCCGGGTGTTCGTGGGCCTCCTGGGCCGAGCAGATCATCCATTTT}$ ${\tt TTGCATGATCTGCGTGGCCTCGCCCTCCATGCCGGGTTTGATGCGCCATCGCTCCATAACGAG}$ 15 AGGCCCCCCTTGTATTGGCCGCGGATGGTCTGGGTAGCGCTCGCGAGCTTTCGCTTGTGG 20 10 AAGGCGGGTCGGATGGATTTGAGGGTGCGAATCAAGCGGGCGTGCTCTTCGAAGAAGAGACCG TTCGAGAAATCGCCGGTAAACCCGAAAGATGCCGCCGTTGCCCACCAGAGCTGCGTGGAGATC 25 ${\tt GCGAGCGCCTCGGGAACGTCACGGTTGGCGAGCGCCTCCGACAGCCACCTGTGC}$ 15 30 ATTTCCATGGGTTGCAGGGAAGTACCTTTCAGGCTTTCGCGGATCATTCGGTAATATGCGACG 20 35 ATTCCGACGGCCTCGATGGCTTGGGGCAGCGGTAGATGGTATATTTAGCCATGATTTGC CCGAAGATTGCCGCTGCGTCGACAGATCTTTCGCGAGCCGGAACGCCATTTCCACTGCTCTGG 40 25 CTCTCAATATTGAATTGAGCCCTGGCGACTGCCATAGGCCCAGTCGCTCGACACAGTGTACGG AGCGGCCCGATGCTTTCTCCTTTTTTAGTCCTGCACCGAATACTTCTGTTGGGCGCCAAAGAT CCCTTGCCGAGACTGTCCGGCGAGATGTCGTGTGCGAAGCGTCCGCACGTCCAGCGGGCCCAT 45 GCGTTGCTAGAGCATAAAACGGTTCGATGCCTGGTCGAGAGGGAGACGCGAGGAGCCTCCCTT TGGGACGGATGAGGAATTTCGTGACCGAAATGTCGGCAGGAACAGCGGCGCAGAAGCGGCGCA 3.0 TCGATGGGGAACCATGGGTTACGAAGACATTGATGATAATGTCGACGCAATCGCAATCGTCGC

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GATGAGCGGCCGCTTCCCCGGCGCGAGAAACGTCGAGGAGCTGTGGCAGAAGCTCCGCGCTGG $\tt CGTGGAATGCGTCACCTTCACAGAGGCCGAGGCGCTCGCCGCGGGGGTGAGCCGCGAGAT$ 10 GCTCGCGAATCCCAGCTACGTGCGCAGAGGCGCGCCGCTCGACGGCGTGGAGCTCTTCGACGC GGAGGTCGCCTGGGAGGCCCTCGAGCGCCGGTTACGACCCCGATGCCCATTCCGGGCCTAT $\tt CGGCGTCTTCGCGGGCAGCGCCCCGAGCGGGCTACCACTCCCTGGCGCAGTCCGACCCGGAGAT$ 15 CCTAGGCGCCCTCGGCCACTACCAACTGACGCTGAACAACGACAAGGATTATCTCACCACACA ${\tt GCTCGTGGCCGTGGTCATGGCCTGCCAGAGCCTGCTCAACCACGAGTGCGACATGGCGCTCGC}$ 20 ${\tt GGGTGGCGTGGGGATCCATCGGGAGGGGGCTATCTGTATCAGGAGAACGGCATCTC}$ 3.0 TTCGCCCGATGGGCATTGCCGCGCTTCGATGTGGCCGCCAAGGGCACCGTGGGCGGCAGTGG GGTGATTCGAGGAGCGGCGATCAACAACGACGGCTCGAGCAAGATCGGTTACACCGCGCCGAG 25 CGTGCAGGGGCAGGCCGAGGTGATCGGCATGGCCCAGGCGCTCGCCGGCGTGGAGCCGGATGA ${\tt CATCAGCTACATCGAGGCGCACGGGGACGCCGCTCGGCGATCCCATCGAGATCGCAGC}$ 15 CCTCACGCGCGTGTTCCGGGCGAAGACCGCACGAAGGCAGTTCTGCGCCATCGGCTCGAA GACCAACCTCGGCCACCTCGATGCCGCCGCGGGCGTCGCCTCGCTGATCAAAACGGTCATGGC 30 ${\tt CCTCGAGCACCGGAGCTGCCCCGAGCCTGCACTTCGAGCGTCCGAATCCGAAGCTCGAGCTCAGCTCGAGCACTCGAGCTCGAGCTCGAGCTCGAGCTCGAGCTCGAGCTCGAGCTCGAGCTCGAGCTCGAGCTCAGCTCAGCTCAGCTCAGCTCAGAGCTCGAGCTCAGAGCACAGCAGACAG$ 20 35 ATCGATCGCCGATGTCACGTACACGAGCCACGTGGGGCGCGGGCCTGGCCCTTCCGGCGAGC 40 GATCTCGTCATGCCAGGCGGCGAGGGAGGCCCCGTCGTCTTCCTGTTCCCCGGTCAGGGAGC GCAGCACCTCTTCATGGCGCGGGAGCTGTACGAGGTCGAGCCGATCTTCCGGCAGTCCCTCGA CCGCTGCGCGAGCTCCTGCGCGGCCCGGCCTCGATCTGCGGCAGGTCCTCTACCCCGC 45 CGAGGGCAGCGCGACGACGAGCAGGAGCTCGGTAGGACCGCGATCGCCCAGCCCGCGCT GTTCGCCATCGAGCTCTCGCCCAAGCTGTGGATGGCCTGGGGGATCGTCCCCCAGGCGAT GATCGGCCACAGCGTCGGCGAGTTCGCCGCGGCTTGTCTGGCGGGCATCTTCCGCGAAGAGGA

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CGCGCTCCGCCTCGTCGCCGAGCGGGCCGCCTGATGCAACAGATGCCGCCCGGCGCGATGCT 10 GATCAACGGTCCGGCTCTCTCGGTGGTCGCTGGGCCGATCGAGGCCATCGACGCGCTCGCGGC CGAGCTCTTGGACCACGGGCTCTCGTGCCGGCGACTCCACACGCGGCACGCCTTCCACTCGAA GTCAGGCCACTTCCTCTGACCCTGACGGGGGGGGTGGATCTCCCCCGAAGCAGCGACCATCCC 15 $\tt CGCATACTGGGCCCGGCAGCTCGTGGAGCCGGTGCGCTTCGCCCAGGCCGTGAGGCAGCTGCT$ $\tt GTCCGAGTCGACCTCGGCTCGAGCTCGGGCCCGGGCCAGACCCTGAGCCCGCTCGTACG$ 20 GGGCGCCGACCACCTCGCGGTCATCGAGGCGCTCGGCCGTGTCTGGAGCGCTGGTGGGACGGT 10 CGAGCGGCAACGATACTGGGCCTCTCCGCGCCACACGAGCGCTCCGCCGGAAGCGATAATCAA 25 ${\tt GGATCCTCCGGTCTCGACGCGCGCGCGCGCGCGCGCTCTACGTCGTCTTT}$ 15 30 GCTGGAGATCGAGCGCAGGCTGGGCTTCGATAGCCTCCTCCTCCTCGCCCAGGTGATCGCCGC 20 ACAAAGGCATCCGAAGCCGCTGATGCTCGGCGTGATCACGACCCGGGCGCACTCCGTCATCGG 35 AACCGAGATCATCGAGCCCCTGCGCGCTCTGGTGCTCGGCCCCTGCCGCGTCATCCCGCAAGA GATCGCGGCGCCTGATCGCCGATCTGGAGCGAGAGTCGCCCGACTCGGTGGTGGCCTACCG 40 25 CGTGGCTGCAGAGCTCTTGGCCCGAGAGGCGCACGCCACGGCTGATCCTGGTTGGGCGGACAGG CCTGCCAGCGCGCAGGGGTGGGACGACTGGCTCGCGGCGCACGGGCGACGACGAGG 45 CCGAAAGATCCTCCGGATCCGCGCGCTCGAGGAGGCCGGCGCCGAGGTGAAGATCGCCGCGGC CGACGTCTCCGATTTCAATGCGATGCGGAGCGTCATCGAGGAGGCCCGGACGCGCTTCGGCCG 30 CATCGACGCGTCATTCACTCCGCCGGCATCGCGAGTGGAGGCATGATCCAGCTCAGGACGCC

		GATGGCGGCTTGGCGCGTGATGGCGCCGAAGGTCGGCGGCACGCTCGTGCTCGATGCGCTCCT
10		CCGGGACGAGCGTCCCGACTTCCTCCTGATCTGCTCGTCGTTGGCCTCGCTGGTCGGCGGCGC
		CACCCAGATCGATTACTGCGCCGCCAACGCCTTCCTCGACGCCTACGCGCAGAGCCGCGAGGG
		CGAGGAGGGATGCCGCGTCATCTCGGTGCAATGGGACACGTGGAGTGACGTCGGGATGGCGGT
	5	GGACTTCAAGCTCCCGGCCGATCTCCAAGAGGGGCGCCGCGAGAGCCTGAAGCGGGGCATCAG
15		CTCGAGCGAGGCGCCGAGGTGCTCGGCCGCATCTTGAGCGCAGGCATGAGCGGCCCGCTGGC
		GATTTGCACGTCGGATCTACCAGCGTACAAGCAGTCTGTCACGACACGCCGATCGCAGCACGA
		GCAAACTCCCGCCGGCCGATGCACTCGCGCCCAACGACCACGGGAGCCTATGTCGCTCC
		CGAGACCGAGACCGCATCGCCGCGATCTGGCAGGATCTCCTCGGCCTCGAGCAGGT
20	10	AGGCGCAAACGACGATTTCCTCCAGCTGGGCGGCCATTCGCTGTTGGCCACGCAGGTCCTGTC
		TCGCGTCCTGCAGACCCTCAAGGTGGGGATCTCGTTGCCGCAGGTTCTTCGATGCGCCGACGGT
		CGCAGGGCTTTCGCGCCTGGTCGACGCAGCACGGGCCGAAGGCGCCGGACCCGTCGCGCCGGC
25		AATCGGCCGTGTCGAGCGAGACGCCTACCGAATCAAGCCGCCCGC
		CACCAAGCCGTAACAAGAAGGGGATCGAGTCATGGAACCCGTCGGCGGCGTGGACATGAATCA
	15	GCCCGCAAAGCAGCAGGAGACCTGCGTCTTCCCGACCTCCTTCGCGCAGCGGCGGCTCTGGTT
		CCTCGACCAGCTCGAGCCGGGGAGCGCCGTCTACAACATGCCCGCCTCCTTCCGGACGCGCG
30		GCCGTACGACGTCGACTCGCTCGTGCGCAGCGTGAACGAGATCGTGCGCGCCCACGAGTCGCT
		GCGCACGACCGTCGATGTCATCGATGGCGAACCCGTGCAGGTGATCGCCCCCTCGCTGCGCAT
		CGAGGTGCCCGTCGTGGACCTGAGCGAGATCGACGAGCCGGAGGCGGAGGCCCGGCG
35	20	GCTCATGGCGGAGGAGAGCCGCCCCCTTCGATCTCACGCGAGGCCGCTGCTCCGAGCCAA
) 3		GCTGCTCCGGCTCGGCGAGGCCGATCACGTGCTGATCTTGACGATGCATCATATCGTCTCCGA
		CGGCTGGTCGATGGACGTGCTGTTCAAGGAGCTTTCCACGCTCTACGCCGCCTTCCACGAGGG
		CCGCCCGTCGCCGCTCCCGGAGCTGCCGATTCAATACGCCGACTTCGCGGTGTGGCAGCGGGA
10		GCTGCTCCAGGGCGAAGTTCTGGAATCGCACCTCGGGTACTGGAGAGAGCACCTCCGCGGCGC
	25	CCCCACGCTGCTGGAGCTTCCGATGGACCGGCCCCGGCCGCGCGCG
		CCAGCGCGCGTTCCGACTCCCACTCTCCCTGCAACAGGCGGTGCAGGCGCTCAGCCGGCAGGA
		AGGCGCGACCCCTTCATGACGCTGCTGACGGCGTTCAGCGTGCTGCTCTCGCGTTATGCGCG
15		GCAGAGCGATCTGGTGGTTGGCACGCCCATCGCGAATCGCACCCGAGCAGAGCTGGAGGGGCT
		GATCGGCTTCTTCGTCAACATGCTGGCGCTGCGCATCGACCTCGGGGGCGACCCGAGCTTCCG
	30	CGAGCTGCTCGGGCGGGTGCGGGAGGTGACGTTGGGCGCCTACGCGCACCAGGACCTGCCCTT

 ${\tt CGAACGGCTGGTGGAGGAGCTGTCACCAGGGCGGAGCCCCAGCCACAGCCCCTTGTTCCAGGT}$ GTCCTTCACGTTGCAGAACACCCCGATGGATGCGACGAACAGAGCAGACATTGCATCGGGTGG CGCGCCGCTGGTGGAAATGAAGGCGGCGAAATTCGATCTGATCCTGGAGCTCTCGGAATCGCC GCAAGGGTTGCTCGGCACGTTCGAGTACAACACCGACCTGTTCGACGCCGGCACCATCGAGCG GATGGCCGGCCACCTGGAGGTGCTGCTCCCAGCGCCGTCGCGGCGCCGGATCGACCCATTGC GGAGCTGCCGCTCATGGGGGCCGAGGAGCGCAGTCGGGTATTGGTGGAGTGGAACTCCACTGC CAATCAGCTCGCGCATCACCTGCGGAGCCTGGGCGTGGGCCCAGAGGTGCGCGTCGGGTTGTA 1.0 CTCGGTGCTGCTCACGCAGGCGTCGCTCCTCTCGAAGCTGCCGCCCCACGGGGATGCAACGCT GGTACAGCTCGACGCGCTGCACGAAGCGCTCTCCAGGCTGCCACACCATACCCCGCGGAGCGG $\tt CGTCACCGCCCAGAACCTCGCATACGTCATGTACACTTCCGGCTCGACCGGGCGCCCAAGGG$ 15 $\tt CGTGCTCGAGCACCGGGCCTCTGCAACCTGCCCACCGTGCAGGCCAAGCTCTATGGAAT$ CGCGCCGGGCGACAGGCTCCTCCAGTTCGCGCCGCTCTGCTTCGACACATCGTTCTGCGAGAT $\tt CGCGCTCGCGTTGCTCTCGGGAGCGACGCTGGTCATGGGCACGGCGGACGAGCTTCTCCCGGG$ ACCTCCGCTGGTCGAGCTGCTGAAGAAGCACGCGGTCACGGCGATGCTCCTGGCCCCTACCGT GCTCGCAGCGCTGCCAGAACAACAGAGCGCGGCGTTGCCGCTGCGCGTGCTCACGATGGCCGG 20 TGAGGCGTGCCCGGCGGAGCTCGTCAAGCGCTGGAAGGCACCCGGACGGCGCCTGTTCAACTC CTATGGCCCGACCGAGCGACCATTTGGGCAAGCTCCGCAGCGGACCTGTCCGACGAACGGAT CCCGCCCATCGGCCGTCCGATTGCCAATACGCAAATCTACGTGCTCGACGAAGCGCTCGAGCC GGTGCCCATCGGCGTGCCGGGCGAGATCTTCATCGGCGGGGTGGGCGTCGCCCGGGGATATCA CGGGCGTCCGGACCTGACGGCCGAGCGATTCGTACCCGACCCCTTCGGGCAAACCAAAGGGGC . TCGAAACGACGAGCAGGTGAAGGTCCGCGGTGTCCGCATCGAGCTGGAGGAGATCCGCGCGGC GTTGCTCAAGCACCCGGCGGTCGCTCAAGCCGTGGCCGTGGTGCGCGAGGACACGCCGGGGGA CCAGTCCGTGAGCGACTTGCCTGCGACCATGGTGCCATCGTCCTTCGTGGCGCTCGACGC

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10 GATGTTCCAGCACCAGACCATCGCCGAGCTTTCGACCGTGGCTAGAGCCGTCGAGGCGGTCCA CGTCGAGCAGGACCCGGTGACCGGTCCCGCGCCGCTCACGCCGGTGCAGCGCTGGTGGCTGGA ${\tt GCAGGAGGCGGCCGAGCCACTTCAACCAGTCGATCTTCCTCGAGGTACGCGAGCGGCT}$ 15 $\tt CGACGAGAGCGCGCTGGAGCAGCCATCGGCGCTCTGATCGACCACCACGACGCGCTCCGGTT$ GCGCCTCGCGCGCGACGAACGCGCCCCACCAGGTCTTCGCCGCGCGGGAGGCTCGACCCC ATTTCAGCGCGTCGACCTCGGGGCGCTGCCCAGCGCCGAGCAGATCTCCGCCATGGAGAAGGC 20 $\tt CGCGAGCGAGCGAGCCTCGATCTGGCCGCGGGCCGGTCGTCCGCGCCGTGCTCTT$ 10 GGCCGTACGCCTGCCGCCCAAGACCACGTCGGTCAAGCGCTGGGCCGAGCTGCTCACCGAGCA 25 ${\tt AGCTCCGCTGGCCGGGATCGACGGGCCGGCGAGGACGTGTGGGGCTCGGCGCGCCACATCGT}$ 15 CGTCTCGCTCACGCCGGAGCAGACGGAGCAGCTCCTGCGCGAGGTGCCGCAGGCGTACCGCAC 30 ACGGATCGACGGCGCTCCTCACTGCGTTCGCGCAGGCCATCGCTCGGTGGACGGGCTCGCC GGCGGTGCTCCTCGACCTCGAGGGTCACGGGCGCGAGGAGCTCGCCGGCGTAGACCTCACGCG ${\tt CACGGTCGGCTGGTTTACGGCCATGTACCCGATCCTACTCCGCGTCGACGCGGCGGATCCGGG}\\$ TGAGGCGCTCAAATCGATCAAGGAGCAGCTCCGCGCCGTGCCAGGCCGCGGGCTCGGCTACGG 20 35 $\tt CTTGTTGCGTTACCTTCGGTCCGATACCATCGCCGAGGTCCGCGCGTTGCCGCAGGCCGAGCT$ GCGCGAGTATCAAGGCTCGGAGCGCAGCCCGGCGCCCATCGCGCCCACCTCATCGAGGTGAA 40 CGAAACCATCGAGCGCGTCGCGGCGAGCTTCGTCACGGCGCTCCGCGCGCTCATCGCGCACTG CACCTTGCCCGAGGTCGGCGGCAACACGCCTTCCGACTTCGACAAGGTGCGCCTGCGCCAGGA GACCATCGATGCTCTCGACGCAATCGACGCGGGCCCCGGGCCGTCTGCGAGGGGGAGCCGAAT 45 CGAAGACGTCTACCCGCTCTCGCCGCTCCAGGAGGGCATCCTGTTCCACACGCTCTACGCCAC CGATTACACGGCGTATGTCGAGCAGTTCCACTGGACGCTGGAGGGCGATTTCGACGCCGAGGC ${\tt GTTCACCCGCGCCCTCCAGGACGTCGTCGCTCGCCACGTCGTTCGCCTG}$

 ${\tt GGAGCGCCTCGATGCTCCACTTCAGATCGTCCGCACGGGCGCGGTCCTCCCCGTCGAGCACCA}$ GGACCTACGCGGCCCGCGGAGGAGCAGACCGCGCACATCTCCCGTTACGTCGAGGCAGA · 10 GCGCCAGCGCCGGTTCGATCTGCGAAAGGCGCCCCTCATGCGCGCCCGGGCTGCTCCGGCTCCG CAAGGACGCCTGGTGGTCGAGACCATCCACCACCTGATCCTGGACGGCTGGTCGACACA AATCTTGCTCAAAGAAGTGTTCACGCTCTACGAGGCGCACCGCGGACACCGTGGGCATCTCGC 15 GGTGCGCACCGCGGCCTTCTGGCGGCGCGAGCTCGAGGGCTTCTCCGCGCCGACGCCGCTCGG CTCGGGCGACGACGCGGCCCGGCTCGCCGCCTTCGCGCGTCAGCATCAGCTCACGATGAGCAC 20 GCTGGTGCAAGGCGCGTGGGCGCTGCTCTTGTCACGCTACAGCGGCGATCCCGACGTGCTCTT 10 $\tt CGGTATGACCGTCTCGGGCCCGCTCGGCGCCGATTCCCGGTATCGAGCGCATGACCGGCCTCTT$ CATCAACACCATTCCGGTGCGCGTGCGCGAGCCTGCCGACGCGTCGGTGCTCGCGTGGCTCAA 25 GGCCCATAGCGACGTGCCGCGCGGGACCCCGCTCTTCGAGAGCCTCGTCGTCGTCGTCGAGAACTA 15 $\tt CCGCATGATCGATGCGCAGTATATCAGTGATCCACCGTATCCGCTGACGGTCGTCGCGGCCTT$ 30 ${\tt CCATGGGACGCTTTATCTCAATATTGGCTACGAGCGCCGCCGGTTCGACGACCAGGCCGTCGA}$ ${\tt ACGGATGATCGGGCACGTCACGACGCTGCTCCGGGGCTTCGTGCAGAGGCCCGAGACGTCGGT}$ GGCCGCGCGTATCCCGAGGGCCATTGCATGCACGAGCTGTTCGAGCAGCAAGTGGAGCGGTC 20 35 GCCCGAGGCGACCGCGGTGCTCCTCCAGCAGCAGACGTTGACGTATCGAGAGCTGAACATACG CGCCAATCAGCTCGCGCATCACCTGCGGAGCCTCGGCGTGGGCCCAGAAGTGCGCGTGGGCTT 40 25 GCT33TACAGCTCGACGCGCTGCACGAAGCGCTCTCCAGGCTGCCACACCATACCCCGCGGAG CGGCGTCACGGCCCAGAACCTCGCATACGTCATGTACACTTCCGGCTCGACCGGGCGGCCCAA 45 GGGCGTGCTCGAGCACCGCGGCCTGTGCAATCTGCCCACCGTGCAGGCCAAGCTCTATGC AATEGCGCCGAGCGACCGGCTCCTCCAGTTCGCGCCGCTCTGCTTCGACACATCGTTCTGCGA

 ${\tt GGGACCTCCGCTGGTCGAGCTGCTGAAAAAGCACGCGGTCACGGCGATGCTCCTGGCCCCTTC}$ GGTGCTCGCAGCGCTGCCAGAACAACAGAGCGCGGCGTTGCCGCTGCGCGTGCTCGCGATGGC 10 CGGCGAGGCGTGCCCGGCGGAGCTCGTCAAGCGCTGGAAGGCACCCGGACGGCGCCTGTTCAA GATCCCGCCCATCGGCCGTCCGATTGCCAATACGCAAATCTACGTGCTCGACGAAGCGCTCGA 15 TCACGGGCGGCCGGACCTGACGGCCGAGCGATTCGTACCCGACCCCTTCGGGCAAACCAAAGG $\tt GGCGCGCTGTATCGGACCGGCGATCGGGCGCGCGCTGCCGGACGGCAACCTCGAGTTTCT$ 20 10 GCGCCAGTCCGTGAGCGACCGATTGCCCGCGACCATGGTGCCGTCCTTCGTGGCGCTCGA 25 CGCCGGCGGCGAGGACCACGTCGCACCGCGCAACGCCATCGAGGAGGAGCTCACACGAATCTG 15 TTCCCTGCTGCTCCGGGTGCATGATCGGCTCGGCCAGCGGTTCGATCGGCCGCCCTCGAT 30 GGTCGACCTCTTCACCTATCCGACCGTGGCGTCGCTCGCGCGGTTCCTTGGCGAACGGGCGAA CGGCAAGCAATCGCCGAGGGAGGCCGCGGCGGCGGCGGCGGCGCCTGGA GGCGCGGGCGGGGGGGGAAGGCCATCCGTGGCCCGACCTGACCCGGGCACCCTTCCAAGCC CCGCCGTTCCTCGCACATCCGCCGCCTCGAGCGCCGCCGTCCAGCGCCGCCGTTCGCCGACGAG 20 35 GAGGCGCGAGACGACGGTCCAAGGCCTTCGTGGGCTCTTTGCCCCGCAATCCGGAAGCTGCGC GGCAGTTCGTCGCCCTGCAATGCTGCCATTGTAGAGCTCCTCCGCTCGCCGCGGCCTCTTTT CTTGCGGCCCGTCCGCGATTGACCTCACATCCTGATCCCTTCTTGCGTCGTCCAGAAAGTGAT TGACGGCCAGCGCGCGCTTGAGATCTTCCGGCGCGCGGCGATTTCATCGCTCCGGCGCGCCG 40 25 TCGCGACGCTTGCCTTCGTCCCGGCCTGCAGCCCGAATCACGGTGAGGATGCGCCCTCCGTGA CGTCAGCAGAGAGCGGCGCGGCGCCGAGCGCTGACTGCGTCGCGCTCGGGGCGAAGCTCCAGG 45 CGGCGCTGGACGCGCCGCCGCCGCAAAAGGCTCCGGGAGCCGCAGCGGCGGTCCAGAGCG GGGACTGTGTCTGGCGGGGGCGCCACGGGCGTCTCGGACCTGGTCGCGAGCACGCCGACGAAGC $\tt CTGGAGATCTCTTTCGGATCGGCAGCATCACCAAGACCTTCGTCTCTACGCTGATACTCATGC$

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TCCGGGCAGAAGGCCGGTTGTCGCTCGACGACGCGGTGTCGAAGTATGTGAAGGGCATCCCCG ${\tt CCGGCGACCAGATGACGCTGCGCCAGATCCTCGGTCACACGAGCGGGCTCTTCGATTACACGT}$ 10 ACAGCCCGGCGCTCGGCCAAATGATCGAGGTGGATCCGACCCGCGCCTTCGCGCCGGCAGAGC TCATCGCCCTCGCCACGGCCGAGGCGCCGTATTTCGCGCCGGGCGCGGGTTTTCGCTATTCGA ACACCAATTACATCGTGGCCGGCCTGGTGGCCGAGGCGGTGTCGGGGGGACGCTCGCCGGGC ${\tt TGCTCCGCACGCGCATCCTAGACCCTGTGGGCCTCGCGCACACGTATCTGGACGCGCCGAGC}$ 15 $\tt CGCCGGTCCAAGGGCTCATCCGCGGCTACGGCGACTACGGCGCGGGCTTGGTCGACATCACCG$ ACCAGCTGTCGCCCACCGAGGCGTGGGCCGCCGGCGCCCTGGTGTCGAACGTCGATGACCTCA ATCGCTTCTTTGCCCTGCTCATCAGCCACGAGCTGCTCTCGTCGGACGAGCTTCAGGACATGA 20 CCACCTGGACCCCGACGATGTGGCCCCACGAGCCCGGATATGGCCTCGGCCTCATCGAGCGCG ATTCTGCGCTCGGCTCCCTCAACGGGCACTGCGGAATCATCTGGGGCTTTCAATCGGCGTCGT ACGGGGTGCCCGGCCGCGACGCGATCACCGCGCTCATCAACCGGAGCGACGGCGACGCAG CGCGGCTCGTCGACGAGCTCGCGAAGGTCGTGAAAGAGCGCTGATCGAGGCGGAATGGGAGCG 25 15 $\tt CTCGGCGCGTCTCTCGCCGCACCCGCCGCTTGCCGAACACGTAGAGCGGCAGGCCGACGGCG$ 30 CTGCTGTCGTCGTGGCTCGCGAAGACCAGCACCGCCGCCGCTGAGGATGGCGGCGCCCCAGG GTCGTGAGGACCAGGATCACCATGACCGGGCTGTTCCACTCCGTCGTCCGCTCCTCG 20 35 GCGACAGAGGCGCCGACGCCGGGGTCGAGGCGGCGCCGCGGGCGCCGCCGCGCCACGGAA 40 25 GCCGCAACCGCGCGCGGGGCGCGAAGCGGAGGTGGACCTGCTCCATGCGCGCAGCGTCGCCC 45 CTCGACAGGGCCGGGTCAAGGCGCGGGAGTCCGAGAGCCACGAGAACCTCCGCGCCGCAGGAAAC ${\tt GCCTCCCTTCCCCGGCGGGCCGCGCGCGCGCGCGCGCGGGGCCACGCGGGGGCAGCTCCTGGAAGTGCCGCT}$

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 ${\tt CCACCGGGCCGAGGTCGATGCCGTCCATGAACGACGTGAACGCGAAGTACGGCAGCAGCGTCT}$ 10 GCAGCCCGCCGAAGGACCGCGGCCAGGAAGGCGTAGACCTCGAGCAGCCCGGCCAGGTAGC AGGCGTCCTTGGTGAACGGCGCGCCGCCGCCGCGCACACGCGCTGGGCGT 15 GGGGCCGCCGAGCGCAGGAACGCGCACCGCGCGCTGCGCCGCTTGTGCGCGGTGAGCG 20 10 ${\tt CGTGCGTCTCGACCTCGTGGTGCCACAGCCCCTCGGCCTCCCACGCCGCGAAGGTCGCCTCCG}$ GCCGGATGCGGACCCGGCTCATGCCGGCGACCACCTTGGCCGTGACGCGCGGGTCGACGGTGA 25 15 30 TGGCCCCGAGGAGCTCGCGCAGCTCGGCGACGCCGCGCGAGGCCGTCGCGATCGACGCGGT ACTCGACCTCGGGGGGGGCGCGCGAAGAAGCGCTCCTCCACCTCGCGCGGCC ${\tt AGGCGATGTCCTCGAGCAGCTTGAGGGCCTTGCCCTCCGCCAGGCGGCCGCCCACCCGATCGA}$ GCTGCTCCAGCACGCCGCGATCGATCCTCATCGAGCGCAGATCGCCGAAACCGCGAGACGCC 20 35 GGAACCGTCATTCCCTCGACGAGGCAGCGATTGCCATGTTCCGTCGCTTTTTGGAGCGCCGTC CTGGCTCGAGAGCGTCCTTTGGCCCACACCCGAGACACGAATGCTCCGCGCCGAGCGCGGTTG ACCGTGGACCCGCCGGAGAGCCGATGATACGGTCCGGCCGATGTCGGAGAGTGTAGCTCAACT 40 CGAAGAACACCGCGCGCGCTCACCGGACACTGCTACCGGATGCTGGGTTCGGTGGTCGACGC 25 CGACGACGCCGTCCAGGAGACGATGGTGCGCGCCTGGCGGAGCCTGGATAAGTTCGACGGGCG CTCGTCGCTGCGCACCTGGCTGTACCGCATCGCGACGAACGTCTGCATCGACCTGCGGGCCGA 45 $\tt CCGCGCGCGGGGGGGGCGCCCCATCGAGGAAGGCCCGGTCGGCACGGTGGACGACGCGCTCGA$ GACGCGCCGCGCACCCACTGGCTGGAGCCCGTCCCCGACGCGCACGCCCTGCCGGCGGACAT

GCACCTGCCGCAAGCAGCGCGCCGCGCTGCTGCTCACGGAGGTGCTCGGCTGGTCCGCCGC 10 GGCGACGCTCGCGAGCCGCGATCTCGGCGACGCGCCCCCTCGCTGCCGGAGCCGCAGTCCGC GCTGCTCGACCGCTACGTCAACGCCTTCGAGCGGTACGACGTCGACGCGCTCACGGCGCTGCT GCACCAGGACGCGACCCTGTCGATGCCGCCGTTCACCCTGTGGCTCCGCGGCCACGAGTCGAT 15 GAGCGGCTCGCCCGCGTTCGCGCAGTATCGCCCGGCGCCGGAGGGCCGCCACCGGGCCTGGGC GACGCTCTTCCCGCGGTTCGGCCTGCCGTCGATCTACCGGCGTAGCCGCGGGGCGCCCTGCCT 20 10 GCCTCGCCGCGGGTGCCCTGCCTAGCCGCGGGCGCCCGGCCTGGCCACGGGCGCCCGGC $\tt CTGGCCACGGGCCCGGCCAGCGACGGGGCGACGATTTTTTTCTGAGCGACCGATGAGTCCT$ GACGGGGCCGGGGGTCTACGGGGGTGAATCCAACACGGAGGCACCCATGACCGTGACCATCGC 25 ${\tt GGCCACGCTGTTCCTGACGTTCGACGCCGCGGTGAAGGTGCTGAAGCTGTTCCCCGCGGAGGC}$ 15 GTCGACCGCCGAGCTCGGGTTCCCGGCGCACCTCGTCCCCACCCTCGGCTACCTCCAGATCGC TTGCCTCGTGGCCTACCTGATCCCGCGCACCGCGGTGCTCGGCGCGATCCTGTGGACCGGCTA 30 CCTGGGCGCGCGATCGCGATCCACGTGCGGGTCGAGAACCCGCTCTTCAGCCACACGCTCTT ${\tt GCTGACCGCGAGCCCGTCGTCGCAGGGCCGATGAGCTTCACGTTTCACGAGAGTCCATCACGG}$ 20 35 TAAAAGGAGAAGCGAGCCATGACCACAAAGAACCCCCGCAAGCTCTTCGTCAACCTGTCCGTC $\tt CGCGACCTGAAGCGATCGATTGGAGTTCTTCAGCAAGCTCGGGTTCGAGTTCAACCCGCAGTTC$ ACGGACGAGAAGGCCGCCTGCATGGTCGTCAGCGAGGAGGCCTATGTCATGCTCCTCGTGGAG ${\tt TCGTTCTTCAAGACGTTCATGAAGAAGGAGGATCTGCAGCACGGAAGGGCTC}$ 40 TTCGCGCTCTCGTGCAGCAGCCGGGCCGAGGTCGACGACATGGTGAAGAAGGCGGTCGCGGCG GGCGGGTCGCACGCGATGGATCCGCAGGATCACGGCTTCATGTACGGGTGGAGCTTCTACGAC GTGGATGGCCACCACTGGGAGGTCATGTGGATGGATCCCAAGGCGATCCAGCCGTAGCCGACG 45 GTAGCCCACAGCGATGCAGTATCCGTCGCGCTTCGTATCGAAGCACGGCTGTTACGGGCGCGT CAGAGCGCGTCGCAGGTGATGCCGAGCCGCAGCAGCGACACGGGCACGAGCGTGGCTCCGATG

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 ${\tt GAGATGAGCCGAGTCTCGCCCATGGTCTCGGGGTCATGAATGGATGAGTAGGGGACTCGCTCC}$ ${\tt TTCGTCACGTCGTGCTCGACGGCGACGCGAGGCCGAGCTCGAAGTGCACGGGGCCTGGACCGGGCCGAGGCCGGAGGCCGGAGGCCGGAGGCCGAGGCCGAGGCCGAGGCCGAGGCCGAGGCCGGCGCGAGGCCGGCCGAGGCCGAGGCCGAGGCCGAGGCCG$ 10 AAGATCCAGCTCGCCCGGCGCGAGCCCCGACGAAAAGCGTGTCGCCGTCGACGCCAGGGCCG ${\tt AGTCGAAGTCCGACCGCGCCGACGCCGACGCCGACGCCGAAGCTC}$ 5 15 $\tt GTGAGCGCGAGATTGAGGTGCACCCCAGCGCTGTCCGAGCCCGAGTAGAGGCCGGCGCCCACC$ TCCTGCGCGCGGGCCGTCCCGACGCAAAGAAGAAGGGGCTGTCGCGAAGAATCCAAGCGAGATC 20 GATCGAAGTGAGCGCATGTCGGGCCCTGGAGCATCCGCTGTACCAGGTGCGTCGTATTCATGC 1.0 GGCGCGCCGCCGCCGCGCGCTGGCCTGTCCGACGCGAGATCACGAATCCGCCATCGCT $\tt CCCCTGGGCCGGCCGCTCTGGTTCGCCTGCGGGCGCTCGTGTGGCCCATG$ GCAACCTTGTCGCGGTGTCGCTCGAACAGCACAGAGAGTATCGCGTCCGCAACAACCGCGCGA 25 CCCGGCGAGACGCTCGTGGGGCCCCCTGCCTCCCCACTTCATCATAACGCCATCAGGAGCACT $\tt CGACATTTCATTTCTTCACCTCCACTGGCTGAGGGGCGACGGTGCTCGTCATCGGCCGGTTGCT$ CTGGCGGTTGCTCTGGCGGGGTTTCTGACGCCCGGAACTAACGCTTCGAGCGCTCCCCCTTGC 30 TCTCCCGTTCCTTCAGCTCCTCCAGCAGGTCGTCGAGGCGCTCGTAGCTGCCTTCCCAGAAGC GGCGGTAGTTGTCGAGCCAGCCGCTGGCGTCCTCGAGCGGCTTGGCCTCGATCCGACAAGGCC AGATCGCGGGCTGGCTCATCGCGAACGGCTTCGCCAGCTCGCCGACGCCTCGCCGGACG 35 CCGCGCGGCTACGTGCGCGCGGCGGGGTGAGCACGTCCTGCAGCGTGGCGCCGACCACGGGCTTG 40 GTCAGGTGCAGGTCGAAGCCGGCCCGCCTGGACCTGGCCTGATCGTCGGGCCCGCCGTAGCCC 25 TAACCGTCGATGCCGGGCAAGCCGATGTCCACGAAGGCCACCTCGGGGCGCAGCTCCAGAAGC 45 TTCTTCACGCCCTCCAGCCGTCCACCGCCACCGTCACCTCGTGCCCCAGCGCCTCGATGTAC GCCCGCATCACCCGGCGCACGTCCTCCGCGTCCTCCACGACGAGCACCCGGCGCCGGTCAGCC

10 CTGCCGCCGTGCAGTTCCAGGAGCCGCCCGCCCGCCCGTGAGCCCGAGCCCCAGCCCGCCGTG GGGATGCCGCGGCCCGTGTCGCGCACCCGCAGCACGGCCTCGGGCGCCGACCGCCGCCTCG 15 CGCGTGAGGCGCACCGAGATCGAGCCCCCGGCGGGGTGTACTTCGCGGCGTTGGTCAGGAGG TTCGTCACCACCTGCTCCAGCCGCGTCGCGTCGCCCATGCCGAAGTCCCCGGGCCCCACC ACCACCGCCGCGAGATCGACGTCCTCGAGGCGCAGCTCCACCGTGCCCCGCGTGATGCGCGAC 20 10 ACGTCGAGCAGATCGTCGACCAGCCGCACGAGGTGGCCCATCTGCCGCCGCGCGATCTCCCGG TAGCGCGCCGACGCGGCCCGTCGCCGTCGCCGACGCGACAGCCTCACCGACAGCCTGATC GAGGCCATCGGGTTCCGGAGCTCGTGCGCGAGCATCGCGAGGAACTCGTCCTTGCGCTGATCG 25 TCGAACGCGAACACGAAGACGCCCTCGACCGCCCCGTCGCGATCGCGCATCGGCTGGTAGACG AAGTTGAAGAACACCTCCTCCGTCGTGCCGTCGCCCCGGGGATCGAGCCGCACCGGGAGCTCC $\tt TTGCCGACGATGGGCTCGCGGTGCGGACCACCGCGTCGAGGAGCTCCCAGATGCCCTGTCCC$ 30 GGGGCCTGCATGAAGAGGTCGTTCAGGTACTGGCGCTCGCCCTCGGCCTCGCGCCGGCGGCGC 20 GCGAGCTCGACGTGGATGCGGACCCGCGCGGGGGGGGGCTCCTTCGCGGAGAACGGCTTCACGAGG 35 ATCACCACGGCGACGCCGCGGGTGCGATCGTCGGCGCGCAGCGCCCTGAGCAGGCCGAAGCCG AGGGCGGCCGACGTCGGCCACGGCCTCCACCGTCCACCCCTCCGCCACGAGCAGCCGCAGC 40 25 GGCCCTCGCCGGCCGGGCGGGACGCCGGGGCGCCTGCTCGCCGCGGAGCCACTGCGCGGCCTCG 45

or its complementary strand,

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(b) DNA-sequences which hybridise under stringent conditions to regions of DNA-sequences according to (a) encoding proteins or to fragments of said DNA-sequences,

- 5 (c) DNA-sequences which hybridise to the DNA-sequences according to (a) and (b) because of a degeneration of the genetic code,
- (d) allele variations and mutants resulting by substitution,

 insertion or deletion of nucleotides or inversion of nucleotide segments of DNA-sequences according to (a) to (c), wherein the variations and mutants offer isofunctional expression products.
 - 7. DNA sequence according to claims 1 to 5, wherein the DNA is selected from the group consisting of
 - (a) the following DNA Sequence:

Seq ID No 2 (>pEPOcos6 region)

 ${\tt TCGAGGCGCTGCTGGCCAAGAACATCGCCCGCGCGCGCGGCGACAACTATCGCCGCTTCCTCG}$

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ATGCGGAAGTCGAGCCCGGTCGGGCCGGAGGCGCACCATGACGAGCGCGGTCCCGACGCGTCA AACCAGCCTGCTCGACGACTTCGAGCGCGTCGCCGACGTCGATCCAGAGCGGATCGCCGTCCA 10 GCTACGGGCGCGGGATCGGGCCCAATCAAATCGTGGCGGTGGCGATGGCCCGCACGCCCGA GCTGATGATCGTGCTGTACGGCATCCTCAAGGCCGGCGGCGCCTACATGCCCATCGCCCGCGA 15 GCCGGACCACAACCCCGAGCCGCGTCACGACCCGACCTGATTTACGTCATCTACACCTC GGGCTCGACCGGCCAGCCCAAGGGCGTGGCCATGGAGCACCGCGCGTGTGGAATCGCCTGAC . 20 10 ${\tt TTGGATGCAGGCCCAGTATCCAATCGACACGCAGGACGTGATCCTCCAAAAGACGCCGATCGT}$ $\tt CTTCGACGTGTCGGGAGCTGTTCTGGTGGCCGCTGGCCGCGCCTCGGTGGCCCTGCT$ GCCGCAATCCATGGAGAAGTTCCCCTGGGCGATATCGGCGACGGTGGCGCGGTGCGGGGTGAC 25 GATGGCGGACCAGATGAAGGGCCTGCGCTACGTCTTCTGCAGCGGCGAGGCCCTGGCGCCGGC 15 CCACGTGTCAGCCTTTCAGGAGCACATCAACCGAGCGGGCAGCATCAGCTTGACCAACCTCTA 30 GCGGGTGCCGATCGGACGACGATCACCGGCATCCAGCTGCTCATGCGCGACGGCGTGCC TCAGCCGCCCGGCGTCGAGGGTGAGCTCGCCATCGGCGGCGTTGGTTTGGCGCGCGGCTACAT 20 35 CGACCATCAGGTGAAAATTCGCGGTCTGCGCATCGAGCCCGGGGAAATCGAGGCCCAGATCAG GCTGACCGCCTACATTGTCGTGGCGCGACCGGGCTTGACCCGGAAGGCGCTGCTACAGTTCCT ${\tt GGGCGCGGCTGCCCGACTACATGCTCCCGAACCGCTTCCTGACCCTCACGGAGCTGCCCGT}$ 40 GACCGCCAACGGTAAGCGCGACTGGCGCGCGCTGCTCGGCCCCCTCGAGACCCTGCCTCTCCC 25 45 CGGGCGACCATCCAGGCTGGGTCCTGGTGGACCGCGAGCCCGAGCCGCGCACGGCGCTGCTGT GGGCCTTTTCCGATCGGCTCTTCTGCGTGGGCGCAGCTGACACGCTGACCCCGCACGCGCTGG ${\tt CCGAGCTGTTCCACGACCGACTGATCCCCCAGGCCCGTAAGATCGGGCAGCCGTTTTTCCAGG}$

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10 AGCTGGCAGAGGCGCGCTCGTGCCAATCGACGCGGCTGCTGGCCGAACAGGCTGATCTGC ${\tt GCGAGCGGATACTGGCCTCCTGGTCCAGCGAAGCTGCCTTCCATGCGCGCGGTTTCGGCTTCT}$ GCTACCGCGTAGGTGACCAGCTGCCGAGCGTGTGCCTGGCATCGCACGTAGGCGGCGGCGCGG $\tt CCGAGCTGAGCATCAACACCGAGCTCGAAGCGCGCAATCGAGGTATGGCAACGCGGCTGTGCC$ 15 GGCGTTTCATCGCCGAATCGCTGCAGCGCGGCCTGACGCCTTGCTGGGGCACCGAGACCTTTC GCCTGCCGTCAATCGCGCTGGCCCAGAAGCTCGGTTTCATCCCGACCTTCACCTTCCCCACCT ACTGCTTCGCGACCGGCACCGAACAGCCGGACGACTTCCTAGGCGAGCTGTACTACAGGG 20 10 ${\tt AATCGCGCATCGCCGGAAGTGGGACCGATGAGCCGCAAGCGGTTCGGCTGGCGCGGGGTTGGA}$ GCCTGGCCGGCGACACCGAGCGTGCCGCAGGCTTCGCCGCACGCGCCCTGGCCGAAGGGTGGG ${\tt CCCGCCTCAATGTCCCTTGAAAGGTCACGTGGACTCATGATGTCCCCTTGAAAGGTCACACTC}$ 25 ${\tt CGAGTCATGATGATTTGTCACTCCCACCGCTTCATTTTCCTCCACGTTCCCAAGGTCGCCGGC}$ 15 ACAAGCGTCAAGGACGTCCTCGGCCAAGAGCTATTCCAGGAGGACCAGGTCACGTTCCAGATC GCTCCCAATCCCCACTACCCACCTGAATGGACTGCGCCTTACGAGGAGCACATTATTGCCGCT 30 GAATTGAAGAGCCAGTTGGCGCCGGAAATTTGGGACGATTACTTCAAGTTCGCCTTCGTGCGC CATCCGCTCGACTGGGCGGTCTCCAATTACTTCTTCTTCCTGCGCGACCGCAAAGGCCATCCG GCCCACGAATTCCTGGAGCGGAAGGGCTTCGCCGGTACCATGGACATGTTTTTCGGAGCGGCC 2.0 35 GGCCGGACGCTGGTGGACTTCGTTGGCAAGTACGAGCGGCTCGAGCAGGACTTCGCCGCCGTG TGTATCCGCATCGGGCTGACCCCGCCCGACTTGCCGTGCCTCAACCAGACTCGCCACCAATCC TTTACCAGTTACTACGACGAGGCTTTGATGCGCCAAGTCAGCCGCGCGTTAGCTCGCGATTTC GAAATTTTTGATTATGCCTGAGGCGGACCCGTTGCTTCGCCACCGGTGGATTATTCGATAAGT 40 25 TATTATATTTTCAGTTGATCATGTGAATGTCGATCCAGCCAACGAGGAGGATACCTCCGCGTG CGGCTATGGGGGCGCAGAGGTCACGACTACGTGTAGAAATTTGTCGAACACCACCACTAGCTGC CACCGATTGGGAGCTTTGACTTGAAGATGAAAGTGGACAAGCGGAATGTCGACGACATTCTCG 45 GACTCACTCCGACACAGACAGGCATCTTGTACCACTACCTGCTGGACCCGCAGGCCGACGCCT ATTTCGAACAATTGACGCTGCACCTGGAGGGGCCCCTCGACGTAGCGCGCTTCCGCCGCCCCT ${\tt GGGAGCGCGTGGTGGCGGCGCCGTGTTTCGCTGGCAAGGGATCGAAC}$ 30

ACCCGGTGCAGATCATCCTCAAGCAGCACGTGCCGGACCTGGAGTTGGCGGAGGTCCCGCGCG ACGCCGATCCGGCAGCCTTCCTGGCGCAATGGGTCGCGGCCGACCGGGCGCGCAAGTTCGACT 10 TCGAGACGGTGCCCTTTCGCATCGGCCTCTGCCGGACTGATACCCAACATCACGTGATGCTGC TCAGCAATCACCATATCCTGATGGACGGTTGGAGTACGGGCCTGATTCTGCGGGACTTCCTCG ${\tt CCTGCTACGGCGACTCCGAAAACTGGCGGCCACGCACCCGAACGCACTTCAAGGCGTTCATCA}$ 15 CGCCCGACGGCGTTTCCCCGCCTGGGCGTCGAAGAAGGCACCCGCCACTCGCTTGACTTCG GCGCCCGCAGCCGCTCTCGACGACCGCTTGACCCAAGGCTTGCGCGACATGGCTCGCGACC ${\tt TCGACGTCACCCTCGCCGCGATGCTCCATACCGCTTGGGGCCTTCTACTCCAGCGCTACCAGA}$ 20 10 ${\tt ACAGCTGCGAAGTGATATTCGGGACCACCGTTTCCGGCCGCCAACGTCGAGCTCGCCGGCCTCG}$ ACGAGGTGGTCGGCTTGTTCATCAACACGATTCCGTTCCGCCTTCTCGGCCGCCGCCGACGA CGCCCGTCGAGGCCTTCCGTGCGGTACAGCGCAATCTGCTGGCGAGAAGCGAGTTCGAAGCCA CCCCGCTGGTGGACATCAAGGGCTGGAGTGGTCTCGGTCCGGGCGCGGAACTGTTCGACACCA 25 ${\tt TCCTGGTCATCGAGAACTATCCCTTGGACCGCGCTATCTTCGAGAGTGATTCCAGCCTGCGGT}$ 15 TGACCGACCACAATCTTCGAGCGCACCAATTACGGGCTGACCCTGACCATCGAGACCTTCA GCCGGTTGCACGTGACGCTAGCCCATCGCCGTGACCTGCTGGGCGACGCGGCCGCTGAGCGAA 30 TGCTAGATCATTTCACCGGCCTGCTCCAAGCCATGCTGCGCTTCCCTCACCAGCCGTTCGCGC GCCTCGAGATGAAAAGCGAACACGAGGCCCACCGCGTCCTGCACCAACTCAACCAAACGCGTC AGCCGCTGCCGATCGGCTTTCCACCAGTTGTTCTTCGAGCAGGCCCAGGCCGATGGGG 35 TGCGTCTGGCGGGACGGCTGCAGGAAGCCGGCTTCGCCCGAGGCGATGTCGCCGCCGTCAGCC ${\tt TCGGCCCGGTTCCGGATCTGATTCCCGGTTTGCTGGGCCCGCTGTTCGCCGGCGCGCCCTACC}$ ${\tt TGCCGCTCGATCCCACCCTGCCGGCCCAGCGCTCGCGGTTCATCCTCGACGATGCCGGTTGCC}$ 40 25 ACACCTCGGGCTCCACCGGCCAGCCCAAAGGCGTCTGGGTTAGCCACCGCAACCTGATCAACT TCCTGACGGGCATGAGCGCAATCCTGCCGGTCGCCGACGACGTGTTCCTCTCGCTGACTA 45 CCGTGTCGTTCGACATTTTCGGGCTCGAGACGTGGTTCCCGCTCAGCCGCGGCTGCACGATCG TCTTGGGCACGCGCGCGAGCAGTTGGACCCGGCCGCGGCTGCCAAGGCCATCTCCTGCCATG GCGTCACGGTTTACCAGGCGACGCCATCGCGACTCCAACTTCAACTGGAGCACCCCACATTTG

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TGCGGCGCGTACGCGAAGTGACCGATGCGCGTATCTTCAACCTCTACGGTCCCACCGAAACCA 10 CCATCTGGTCCACAGCCGGGGAGGTCACCGCGGGCGGACGTCCCGGATATCGGCCGCCCGATCG CAAATACCGGCGTTTTCCTTCTGGCGCGAGACGGCTCGATCCAGCCGCCGGGCCTGGTGGGCG AGTTGTGCATCGCCGGCGAGGGCGTGGCGTTGGGCTACCACCGACGGCCGGACCTGAACCGAG AACGGTTTCGCGAGATTCCGCCGGGCCCCCCTTTGCCGGCAAGCTCTACCACACCGGCG 15 ACCTGGCCCGCTGGACCGAAGACGGACGGCTCCTCTGCCTGGGCCGTCTGGACCACCAGCTCA TCACGCAGGCGGTGGTCGTCACGCGGCCGCGAACGGCCGAGCCGGTCTTGGTCGGGTTCTGGA 20 10 GCTACATGGTACCCGAACGGTGCATCCTCATGAAGGCCATGCCGCTAACCGGCAACGGCAAGA TCGACCGGCGCGCCTACCCAATCCCTTCGCCTTGACCGAGTCGACCCGGCAGGCGGCGCCGC GCACCTTGGCCCGCACCGCCGGCGAGCATCGGGTTGCCGAGCTGTGGCAGGCCTTGTTGCGAC 25 GCGAGGCGATCGGCTTGGACGAACCCTTTTTTCAGGCCGGCGGGAACTCATTCGGCTTGATTC 15 GGCTTCACGCCAAGCTGGAATCCGCCTTCGGGAAGTCGTTCCCGATCACCGATTTGTTCCAGC 30 GAGCCGTGCCGCAACCCCCGGCCGCCGCCCCAAGTTGCCTCCTCGGCAGCTAAATCCCCAG GGGAGCGCGGCGGCAGCGACGTCGAGCGGCCTGACCGCGCAACCGCCCAACCCCACTTCC GGCCCATCGCCGTTATCGGCCTCGCCGGCCGATTCCCCGCCGCCCCACCTCGACGCCTTCC 20 35 AGGGTCTCGACGCGAATCGAATCGCGTGTCATAACTATGTCCCGGCCAAAGGTTTCCTCGACC ${\tt GCGGCGGGGAGATCGGGCTCTTCGCCGGCTCCTCGGCCAACTATCACTGGCTCGAATACGTGG}$ 40 25 GCATTTCCGAGGAGCAGCAATCGATTCGCCGTCATGATTCAAAACGAAAAGGACTACCTGG $\tt CCACGCGGATCGCCTACCAGCTCGATTGAAGGGCATTGCCGTCACCGTGCAAACGGCCTGCT$ 45 CTTTGGCTGGTGGCGTTGGTCTGACCTATCCGTTGCGCGCCGGATACCTGCACGAGGATGGAA TGATCTTCTCCCCGACGTCGGTGCCGGGCCTTCGACGCCCAGGCGGCCCGGCACGGTCTGCG GCAACGGTCTGGGCATGGTGCTGAAACAGCTCGACGGCGGCGGCGACGGCGATGCCA 3.0

TCCACGCTGTGATTAAGGGCATCGCGGCCAACAACGACGGCGCGGCCCAAGATCGGCTACACGG 10 $\tt CGGAGACCATCGGCTATGTAGAAGCCCACGGTTCGGGCACGCCGCTGGGCGATCCGATCGAGG$ TGGCGGGCCTGACCGAGGCCTTTGACAGCCCGCGTCGCGCCTTCTGCGCCTTGGGTTCGGTCA ${\tt AGTCGAATGTGGGTCATTTGGATGCGGCAGCGGGCATCGCGGGTTTCATCAAGGCGGTGCTCT}$ 15 $\tt CGCTGTCCCATCGGACCCTGTTCGCCAGCCTCCACGTCGACACCCCGCAGATCCCGT$ TCGCCGACGGTCCGTTCCAGGTCAACACGGAGACCCGGCCCTGGCCAGCTGCCGACCATCCCC GCCGCGCCGGCGTCAGCTCCTTCGGCATCGGCGCACCAACGTGCACGCCGTCCTGGAAGAGG 20 10 ACCTCGCACCAGATGACGTTGCCTTTACCTTGCACGCGGGCCGCAAACCGATGACCCACCGTC GTTTCCTGGTCGCCGACCTCGCGGAAGCCGCCGCGCGTCTGGCCGAGCCCGATCCAGTCA ${\tt AATCCGCCGCGCGCCGCCGACCGCTGCCAGGTCTGGATGTTCGCCGGTCTCGGCTCTCAAT}$ 25 ACCCCGGCATGTGTGGCGGCCTCTATCGCACCGAGCCGGCCTTTCGCGAGCAAGTCGACCGCT 1.5 GTTTCGACCTCCTCGCGCCGCGTTGCGATTTGAAGCCCTCGCTCTTCCCCGAGCCCGATCAGG CCATCGACGCATCAGCCCTCGCGGCCATCGACACCGCCCAGATCGCCGTCTTCGTCTGCGAAT 30 ACGCGCTCGCACGGATGCTGGAAGGCTGGGGGGCTGCGTCCGGATCGGCTGATCGGTTACAGTT TCGGCGAATACGTGGCCGGCCTGCCTGGCCGGCGTCTTCTCCCTGCCCGACGCCTTGGCAATCG TCCGCGAGCGTGGCCGGATCCTGGCGGCGGCCGAGCCGGGCGCGATGGTCAGCGTGCCCCTTC $\tt CGGCCGAGCGCCGCTCGCTGGAGCCGCCGCTTGCCTTGGCCATTGACAACGGCCCCT$ 35 CATGCGTGGTGCGGGCCGGTCGAACCGGTGCGCACCTTCACCGCTCGCATGAAGCGGGACC GGGTCTGGGTGACGCCGCTCCAGGCCGAGCGCCCGATGCATTCGCCGCTGATGGCCGAGGCCG GCGGCTCACTGCGCGCCATGTTGGCCGGGTTCCGCCTGAATGCGCCGCGAATCCCGATCTTAA GCAATGTTACAGGAACCTACCTAACCGACGAGCAGGCCCGAGACCCCGATTACTGGGCCCGTC 40 ACCTGTGCGGCAACGTTCGCTTCGCCGACGGTGTGCGAACCTTGTTGGCCGAGCGCGATCCGG TGTTCCTTGAATTCGGGCCGGGCCGCGATCTGAGCTCCTTGGTGCGCCACCAGATGCCGGAAG GCGCCGACGAGCCGATCGCACTGATCCGTCATCGCGAAGATCCGGTGCGCGACGAAGACCTCC 45 ${\tt CCGGCCGAGGCTGCCGCGTGCCGGTTACCCGTTCCAGGGTCCACGCTGCATGC}$ $\tt CGGCCCGCGCCGGCCTGGCGCGACCGACCGTGGGAGCGACCACCATCAGCTACC$

10 ATCCCCGCGAGGAACAAGATCTCGCACAGCTGTTCGCGACCCTGTCGGCCGAAGCGATGCTGC CCACCCACATCCTGCACCTGCTCAGCCTGCCGTCGCCGGAGCGCGACTCGCCGCTGGCGCGCC ${\tt TGGAGCACCTCACCGAGCTGGGCTTCCACCATCTGCTGGCCCTGGCCCGCCAACTGGAGGCGG}$ 15 ${\tt TCGGCGCCCCGAGGTCCGCCTCGCCGTGGTGACAACCGGCCTGGCGGCGATTGGCGGCGAGT}$ CCGAGCTGCGGCCCGAGGTCGGGCTGTTGCGGGGGACCTGTCCGCGTGATTCCCTTTGAATTCC CGAACTTGCGGCTGCCCTGATCGACCTCGACTCGGCCGATCCCATCTGGCGTAGCGGTTGTG 20 10 AGCCGTTGCTGCGCGAAATGGGCGCTGCCCCGGGACCTGAAGAAATCGCGCTGCGCGGCACCA GCCGTTGGGAGTTGGGCTACGAGCCGGTCGAGGGGGGGGCACCGTGAGCACCATCTCCTCGCGAC 25 GCGAGCTCTGGCACCAGGCGCCAGCGGAGTTCGTACCGGTCGCAGCTGCGATCGCACAGATGG AGGAGTGTGGCGCCCGCGTGATTCCCGTCGCGCTCGACGTCACCGACGCCGACCAAGTGAACG 30 TCGTTGACGGCGCATCATTCGAACGCGCACGCGCGCTGCCAGCGACGCCGTGCTGGCGCCCA AAACGGTCGGAACCTGGATTCTCGATCGGGCTCTCCGGCGCGCCGGTGGCCGCTTCCTGGTGC TGTACTCCTCGATCAACGCGGTCGTCGCGCCCTTCGGCCAGGTTGCCTACGCCGCCGAACG 20 35 CCCCGCTCGAAGGGCTTAGCGACGAGCAGGGCTTGCGCCTGGTCGAAAGCGCCTTGGTCGGTT GCGAACCGCGACTCCTCGTCTCCATCAGCGAACTGCGCGCTCGACTAGCCGAGCATCATCGCA ACGGCGGCATTCCCCGGTTGCTCGGGCCCCGCGCCCAACGAGGCGGGTGCAGCTGATTCCGGCG 40 ${\tt AGGAGGCGCCACGCAAGACGCGTCGCCGGCCCGTCCCGATCTGGTCGTGGCCT}$ 25 TCGCGCCGGCCAACGAGCTGGAGCGCCGGATCGTGGCCATCATCGGCGCCTACCTGCGGC 45 AGATCGCCCAACGCCTCGGTCGCGAGTTGGGCCGCGATGTCCCTGTCGTCTCGCTCTACCAAC ${\tt ACCGCACCGTACGCGGGCTGAGCCGCTTCCTCGGCGGCGCGCTCCAATCCGCGCGCTCCGGCG}$ TCCCGACGGGCGCTGCCGCCACCGCGGCGGCCACGCCGGGGGGTTGCCACCCCGCCGCGGGCCAC 30

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AACCGTCGCGCCAGCACCTGGAAAAACGCCGTCAATTGAGGAAAAAAGGGGGGCCTTCCCATC ATGAGTGAAGTATCCATTCGCCCCGGCTTGGACATCGCGGTCATCGGCATGGCCTGCCGCTTT 10 CCCGGTGCCCGCAACCTCGCCGAGTATTGGGCCAACCTGATCGAAGGCCTCGAAACGCTCAGC TTCTTCAGCGAAGAGGAGCTGCGTGAGGCCGGCTGCGATCCGGTCCAACTGGCCCAGCACAAC TACGTGCGCACCAAGGGCCTGCTCCCTGACGCAGACCGTTTCGACGCCGATTTTTTTGGTTAT 15 TCCCCGCGCGAAGCCCAGGTGATGGACCCCCAGATCCGCGTCTTCCACGAGGTCTGTTGGCAG ${\tt GCGCTGGAGCACGGGGCTACAACCCGCATCGCCACACCGGCACGATCGGCCTGTTCGCCGGC}$ ${\tt GCCGCGCCCAACGTTTTTTGGGAGTTTCTCTCTATCGGTCCGATGCCGCCAATTTAGGCAAC}$ ${\tt TTCACGCTGGGCCTGCACAACAACAACGACTACCTGAGCTCGCGCATCGCCTACAACTTCA$ 20 10 $\tt CTGACAGGGCCCAGCTACACCCTGTTCACCGCCTGGTCGACCTCGATGGTCGCCATCCACCAGGTCGCCACCAGGTCGCCACCAGGTCGCCACCAGGTCGCCACCAGGTCGCCACCAGGTCGCCACAGGTCGCCACAGGTCGCCACCAGGTCGCCACCAGGTCGCCACAGGTCACAGGTCGCCACAGGTCACAGAGTCACAAGAGTCACAGAGTCACAGAGTCACAGAGTCACAGAGTCACAGAGAGTCACAGAGTCACAGAGAG$ GCCGTCCAGGCGCTCAACGGCGAATGCGACCTGTGCATGGCCGGCTCGGTCTCCATTACG $\tt CTGCCACTGGTTGCCGGCTACACCTACACGCCGGGCATGATCGTCTCGCCCGACGGCCATTGC$ 25 CTCAACAACGATGGCAGTCGCAAGACCGGCTACACCGCGCCCAGCGTGCAGGGGCAGGTGGAG GTGATCCGCGCGGCGATGAACCTGGCGGAGGTCGAGCCGGAGGCGATCAGCTACGTGGAAACC CACGGGACGGCCACCACGGTGGGCCATCCGCTGGAGTTCGAGGCGCTAAAGGAGGCCTTCGGA 30 GGTGGCTGCAAGGCCTTCTGTGGATTGGGTTCGGTCAAGCCGAACATCGGCCATCTGGACGTG ACGTCGGGGATCGCGAGCTTCATCAAGCTGGTCCTGGCGCTGGAGCACCGCATCCTACCGCCC 20 ACGCTCCACTTCCAACTGCCCAACCCGAAGATGGATGTGGTCGATAGCCCCTTCTACATCGTG 35 GCTGAGCGCGAACCCTGGCGCGAAGATCTGCTGCCGCGTCGGGCCGGTGTCAGCGCGTTCGGT CTGGGTGGCACCAACGTCCACATGATTTTGGAGGAGTTTCAGCGCGAACCGGCGGCGAACAGC GCGCGCACGCGCCACCTGACGGTGCTGACGGCGCGCGCCGCAAGCCCTGGCGCAGCTGGCG GCCAACCTCGCCGAACACCTGCGCGAACACCCCCGAGTTGGCCCGATGTGGCCCATACG 40 CTGCTGCACGGCCGCAAGCCACTCCATTCGCGCGCGCATCCTGGTGGCGACCGATACGACGGCG 25 GCGATCGACGCCTTGATGAACGACCGCGATCCGCGAACGCGTTTCTTCGAAGCGACCGGGCGC GGCGAGTCGGTGATCCTGTGTTTTGACGAAACGCCGCCGGGGGCCGCGAAGCGCCCGCTACCTC 45 TGGGATCACGAGCCGCTTTATCGCGCGGCGGCGACGTCGTGCTTGGCTGGTGAGGTCGCCGAC CCGGATCTGGAAGGCTGCTTTACTGCCCTGATCGCCGAGCAGCGGCGGCAGCCGCCTTTTGC 30

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10 AATTTCTCTGGAAACTGGATCGTTGGGCGTGAGTTGGCCGGACCCGGATTACCCCAGAAAGCAG AAGGGTAAGCGCTGCATGAAGCGCCGTCGGTCCCAACCTCGGTCAGCTGGTGCAGGATGGGGG 15 GCCGCGGCGAGGCGTGGTCGCTGCCGAAGAAGAGCCCAGGACTTTCTCGCAACCGCAATG 20 ${\tt GATCGCAGCGCTCGCTGGCGTTGTTCTCCAGGCGCAGCCGACCGTCGTCGAGGAAGCGC}$ 10 GGACGAGCGTGCTCGGCCCTGGCCCAGGCAAAGAACGCGTCGACCAGAGGGCGGACGACGACA TCGCGACGCACCTTGCGCTGCGCGGGCGGCAGGTCCGCCAGCGCGCGATCGGCGCAAAGAGG 25 GCGTTGATGCGCCGCAGCCCCTCGACACCGAGCTCGTGCTTGCAGACCGCCGCCTCCCAGAAG 15 GCAGCGCCTCTTGGTGGTGTGCCGCGGAAGAGGGCGTCATAGATGGCGTGAGCGTCAGCTTGA 30 ATATACCGAGAGAAGCCGCGGAACATCTCGCAGACCGCGGCGCTGGTATGCTTGGGCTGGTAC TCGAAGAAGACGTGATCCTTGTCCGCGAGGACGACGAAGAAGTGTCCCTTGCGGCACGGCCCG 20 35 GCACCGACGTCTTCGGCGTAGCGGCACATCGTGCCGCGATCGAGCGCGCCCTGAAGCTCC AGCTGCTGCTCCAGTCGATAGAACGGGACGCCGAGCAGGTACTTGCTGGTGAGGATGTGCGCA ATCATCGACGGCGCGAGGAACGACCGCCGGAACAACTCCTTCGGAAGCGGCGTCGTGATGAAG 40 25 GTGGAGGAAGCGCTCGCCGGCCGCCGCCGCTGCCGTGTCCTCCGGGCTGACGCTCGCAGCGGGC GTCGGCGTCGGGGCTTCTCTCGCGACGACCTGGAGCGGGGCCGCTTCCTCCTCGCCCGAACTG $\tt CTCGCATCCGTGACGGACCGCTCGGCCTTGTACACGACGCGTGCGAGCACGATGCGGCGCATT$ 45 CCGCCGCGCTCGTAGCCGAGTCGCGAGGTCTCCTCGACCCCGATGCGCGTCGCCGTCGCATCG AGCTCGGGGCAGGAGGCTCGATGCGGACGACGGGCAGGTCGGACTCGGACAGGTCGCGACGG

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TTGCGCTCGGCGCGTCGAGTGCCTTCGCGAGGCGCTCGAGCATCGAGTCGAAC GCCAGCTGCTCCGCGCTCACCTCGGCGCGCTCCGCCTTGGCCACGAACAGTCGACGTCGCAGA 10 AGCTGCAGCTGCTCGAGCGCACGGGTGTAGGCGCCGCAAGCTGCGCGAGCGCATCGCGCGCT CCCACGAGCTCGCTCTTTGCCGCGGCGAGCTCCGCTTCGAGCTGCGCGATGCGCTGCTGCTCG GCCGAGAGCGTCGGCTTGGCGGCGCGCTCTGCACGCCGCTCTACGTAAGCCGCGCGTAC 15 TGGGCGCGATCTCGATGCCGTCGAGCAGCGTCTCGAGCGTGGCGTCCACCTCGACGTGCG GGCAGATTCCACTGCCATCGAAGAAGAGAATCTTGATCGTGGTCCGCCGCTTGCCGACGAACG 20 CGAACAGCGCTCCGCAGCCAGCCTCGTACCCCACACGCTCACGGATGAGACCCGAAAGCCGCT 10 TCGCCCCGCTCCGCCGAGGGCACCGACCTCCGCCAGCAGCGCGGGGTCGAACCCCGCGGC GACGCGCACCCGCGCCGCCGACCTCGACGACGAGCTCCGCAGCGCTGCTCGTCACGGCGGG 25 15 GTGCAGCGTCGAGGCCGCAAATCCGCGGCTCCGAGCGAACTCCTCCGCCGTTTCACCACTCTC GCGCCACGCCCGAACGCGCTCGGACCACATCACTTCGGTCGCTTCGTCCTTGTCATGCACGC 30 $\tt CGCGCCGCGCCCATTGTCGGATGCGGTGCGCGACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCTGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGCTGTTGCTGGAACTTCGCCGCCGATCGGAACTTCGCCGCATCGAACTTCGCCGCAACTTCGCAACTTCGCAACTTCGCCGCAACTTCGCAACTTCGCAACTTCGCAACTTCGAACTTCA$ TGGGACAACCACTGGACGTAACGGCTGAAGCGAGCCAACGGCTCCAGCTCGCGCGGGGCGACC 20 35 GACTGTATCCCGACGAACACCGCCGGCGCGCGTGCCGCTGCCGAGCTACCCCTTCGAGGGAAAGC GGTTCTGGATCGAGGGCTCGCCGTTCGAAACCGCGCCGCCGCCGCCGCCCCCCAACCCG CCGATTCGGGGGACATTCTCAAGGGCGACCCGGGGGCTGGTACTATCGGCCGCGTTTCGAAG CGGCGCCGCTCTTGCCCAGCCCGTTCGAGAGCGGAACCCGGCGATTGGCTGGTGTTCGAAGATG 40 25 TCGTTCGAGGCACCGAGTTCCGACGCCTGGCGTCACAGCGCTTCCAGCTTCGTCCCGATCGAC GGGACGATTACCGGACCCTGCTGCACGAGTTGAAGGCGCAGGGCATCGCGCCGGTCCACCTGT 45 GCCACCTATGGAGCGTGACCGCCGCACCGGATGCCGAGCAGTTGCTCGACGTCAGCTTTCACA GCCTGGTCCATTTGGCGGCCGCTTTGGGTTCGGTTGGCTACTTCCACGCCATGAAGTTGAACG ${\tt TGGTCGCCAACCGGGCTATTCGACCCCGAGTCGCCCGAGCGCACCGAGCCCCCAAGAGTCTGT}$ 30

		TGCTCGCGGTGACCAAAGTCCTGCCGCAAGAGGTGCCCAACGTTCGAACCCGCGCCATCAGC
10		TGGACCTGGATCGCTCGTTCGACGCGGCGGCGCCCGCCTGGGCCGCCAGTTTGTTGGTTG
		GCGGCGCCCGTCGAGGAAACGGTGGTGACCTACCATGGCGCAGCCCGATGGCTGCGCCGC
		TCGATCGCGTTGCGGTGAATGGTCTCGGCCCGTTCCACCCCGATCAACCTGCGCCGCTGCTGC
	5	GCGAGCGCGCGTGTACCTGATCACCGGCGGCGTGGCGGCGTGGCCAGTTGGCGCGCC
15		ACCTGGCGCGGCCTGCCGGGCGCGTTGGTGCTCACCGCGCGCCCCGGCCCCTGCCCGAGCGCC
		ACCAGTGGGATCGGGAGTCGGCCGTGCTGTCATGGGACGACAAGACGCGCCAGCGCATCGAGC
		TGGTGCGCGAGCTGGAGCGGCTGGGGGGCCGAAGTATTGGTGGTGGCTGCCGATGTCGCCGACG
20		AAGCGGCCATGGCGCAGGCGATCGAGGCCTCACTGGCGCGATTCGACGCTTTGGACGGCTTGA
20	10	TCCACGGCGCCGGGATCGTGCGGGTCGCGTCGGGCCGCACGCCGATCGGGAGTATGACGCGGG
		CCATGTGCGAGGAGCAGCTCCGCCCCAAGATGTTGGGCCTCGACGTCGTCGACCGCCTCCTGC
		GCGATCGCCGGTTGGACTTCCGCATTGCCATCTCGTCGCCCCCGATTCTCGGCGGCCTCG
25		GCCACGTCGCCTACGCCGCCGCCAACCTCTACATGGACGCGTTCGCGACGCGCGCCGCCGCCGCCG
		GCAACGCGCCTTGGATCGCGCTGAACCTGGCCGAGTGGGAATACGAGGGCCCGGCTACCTAC
	15	ACGAGCGGGTGGGCCGTTCGCTCAAGCAGCTCGAGCTCACCAACGAGGAGGGTATCCGCGTCT
		TCCAGACGGTGTTGGCCTTGGCCGCGCGCGCCCGCTACAGCAGATCATTATTTCCACCGGCG
30		ACCTCCAGGCCCGCCTCGACAAATGGATTCACATCAAATCCCTGCATCGCCGACCGGGGCCGG
		TCCAGCTCAGTCGCCGGACCGCGGCACCCCAGGGCGGTTTCGGCTCGGAGCGCGCCGCCTTCG
		AGGCCGCCTTCGCTGACGCCTGGTGCGACTTCTTCGGGGTTGAAGAGGTCGACCCGAACAAAA
35	20	ACTTCTTCGATCTGGGCGCCAGCTCGCTCGACTTCATCCACCTCGTCAGTCGCTTCAGCAAGG
33		CCATCGAACAGCATGTACCGCTCGAGGCCCTGCTCGAACACTCCACCCTGCACGACCTCGCCG
		CCCACCTCGCGGGCGACGCGAACACCGACGCCAGCGACGAAGCGCGCATTCGCCAACGGCTGC
		AAGGCGCCAAGTCCGGCGACATCGCCATCATCGGCATGGCCGGCC
40		ACCTGGACACCTATTGGCGCAACCTGGTCGGAGGCATCGACGCGGTCAGCTTCTTCAGCGCCG
	25	AGGAGTTGCGTGCTGGCGTCACCGCGGCCGAGATCCACCACCAACTACGTGCCGGCCA
•		AGGGGCGCTGCGCCGACCAGGACTTGTTCGATGCGGCCTTCTTCGAATACACTGCCAGCGACG
		CCGAGCTGATGGACCCGCAAAATCGCGTGTTACACGAGGTCGTGTGGCACGCGCTGGAAGACG
45		CCTGTTTCGACTTCAACGGCGATCACGGCCAGGTCGGCCTGTTCGCGGGCGCCTCGCCGAACC
	•	TGTGGTGGCAGTTCGTGGCCAGCTTTTCCGAGGCCGCCAAGACGCAGGGCATGTTCACCACCA
	30	CCCTGCTCAACGACAAGGACTCGATCGCGACCCAGATTTCATACAAGCTCGGTCTAAAGGGCC

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		CCGCGGTCACCTTGTTCACCGGCTGTTCCACCTCGCTGGTAGCCGTTGACGCCGCCTGCCGCT
10		CGATCTGGTCCGGTCAATCGGACATGGCCGTGGCCGGCGCGCGGCGGGTCTCGCTGACTCTCCCCGATA
10		AGGCCGGCTACATCTACGAAAAGGGCATGCTCTTCTCGGCCGACGGCCATTGCCGGGCTTTCG
		ACGCCAACGCCACCGCATGGTCTTCGGCGACGGCGCCGATCGTGCTCAAGCCGTTGG
	5	ACGCGGCCCTGCGCGACGCGACCCGATCCATGCGGTGATCAAGGCGTTGG
15		ACGGCGACCGCAAAGCCGGCTACACGAGCGTCAGCGCCCAAGGCCCAGGCCGAGGTGATCCGCT
		CGGCCCAGATCCTGGCCGACGTGGCGCCCGAATCCATCAGCTACGTGGAAGCCCACGGTACCG
		GCACCAAGTTGGGCGACTCGATCGAGATCAAGGCGTTGAAGCAAGC
20	1.0	ACGGATTTTGCGGCATCGGGTCGGTCAAGACCAACCTCGGTCACCTGATGGCGGCGGGGGA
	10	TGGCCGGCCTGATCAAGACGGTTCTGGCGATGAAGCACCGCCAATTGCCGCCATCGCTGCACT
		GCGACGAAGTGAACCCCGACCTGGAGTTGGAGCGCAGTCCGTTCTACATCAACACCCGCCTGC
		GCGACTGGGTTGCACCGGGCGGGCCGCGGCGGGGGGGGGG
25		CCAACGCTCACGTCATCCTGGAGGAGCCGCCGACGCGCGAGAGCGCCACGCGCACTCCCACT
		GGAAATTATTGATGCTGTCGGCGGCCAGCGAGGCGGCGCTCGACCGCCAGGCCGATAACCTGG
	15	CCGACTACCTGGAGCGCCATCCCGAGGCCCACCTCAGCGACGTGGCCTATTCCCTCCAGACCG
		GCCGGCGCTTCTGGCCTGGCGGCGCACGGTCCTATGCGAGTACCGCGAGGACGCGGTGACCA
30		GTCTGCGCGAGCGACAGGCCAAGCCCGTCCAGACAAGTCGCGTCCGCTGGGACCACAAGGACG
		TGGTCTTCATGTTTCCCGGTCAGGCCGCCCAGTACCTCAACATGGGCCGCGACTTATACGTCA
		TGGAGCCGGTCTTCCGCGAGGTCATGGACCGCTGCTTCGAGTTGCTGGCCCCTTTGTGGTCCG
35	20	AGCATCCGCCCAGATCCTTTATCC3GAGGGCGGGGTGTCGACCCTGCTCCACCGGACTGATT
50		ACACCCAGCCGATCGTGTTCTGCTTCGAGTACGCCCTCGCCCATTTGCTGCTCTCCTGGGGAT
		TGAAGCCGGCCGACCATCGGCTACAGCTTCGGCGAGTACGTTTCTGCCTGC
		TCTTCTCCCTGGAAGATGCGATCCGTCTGGTGACCGAGCGCGGTCGGCTGATGGCGGCTTTGC
40		CCGCGGGCGCCATGCTCAGCGTCCCGGATGCCGAGCTGCTGCGGCTGCTGGACGGCT
	25	TCCACGCCCAATCGGCGCCCATCTGGCGCTGGCCGTCGACAATGGCGCCTCCTGCATTGTGG
	•	CCGGCGAGCAGGCCGCCATCTCGGCCTTCGAATCGATGCTTCGCAAGAAGCGTCTGTTGACCA
		TGCGGGTCGCGGTCAGCCACGCCGTCATTCGCAGGTCATGACCGGCGCGCACCGACGCCCTGC
45		GCAGCATCCTGCGGAAGATCCCCCTCTCCGCGCCGACAATTCCCTTCATTTCCTGCGTCACCG
		GCACCTGGATCACTGCACAGCAGGCTACGGATCGCGAGTATTGGGTGAACCACATGTGCGGGA
	30	CGGTGCGGTTCGCGGCGGGTCTGACGGAGCTGGGTCAAAACCGCGAGGCGGTGTTCCTGGAAG

 ${\tt TAGGTCCGGGCCGCGACTTGACGTTGCTGGCCCACCGCATCCTGGCCGACAGCGCGGCCGTGT}$ ${\tt TCGAGCTGGTCAAGGCGCCGACGACGACGACGACGATGGGTTCCTCCTGCTGGATCGATTGG}$ 10 ${\tt GGAAACTCTCGCTGCCGGGATATCCGTTCGAGCGGCGCGCTTCTGGATCGAGGGCAACCCGC}$ 15 GTGTAGCGCCAGCCGGGTCGACCAGCGCAGCGGCGCAGACCGGACTGCCCGACACCGA 20 10 $\tt CTGGGGAGCCAGCGGGCTGTGCCAAAGGACGGGGCCGAGCCGGGCCGACCTGGCTTATTTTCG$ ${\tt CCGACGCCGGCGGATTGGCCGAATCTTTCGCCAAGCGGGTTCAGGCCCGCGGCGAGAAGCTTT}$ ACCTGGTGGCTTCCGGCTTCGAGCGCCTGGCCGAGACCCGCTTCCGCCTCGATCCCG 25 ACCTCCTCGACTTCCGCTCGCTTGACTGCGGCGGGCCCGACCCCATGGACCAGGCCG 15 GCTTCTTCGGGCTGTTGCACCTGGTCCAGGCGATGGCAGGCCGGCTACAGCCATCCCATTC GGCTGCTGATCGTCAGTTGCGGCGTCTACGATGTCACCGGTGCCGAACCGCTGCAGCCGGCGC 30 GGGCCACGATGATCGGACCGGCTCTGTGCATCCCGCAACAGTATCCGCACCTCGAAACGAGCC ATGTGGATTTGGGCGTGGTCCATGCCGACGAGCTCCACGCCGCGCGCCAGCTCGACAGCCTAC TTGCCGAATGCCTAAGTGCAACGGCCGAGCGCCCAATTGGCGCTGCGCGGCCGACACCGCTGGC TGCTGGACTACGAGCCAGTCCGCTTGCCGCCGCTCGACCCGGGCCGTCTGCCCTGGCGCCAGC 35 GCGGGGTCTACTTGATCACCGGCGGTTTGGGCGGGATCGGCCGCATCCTGGCCGAACACCTGG CCCGCACGACCTCGCCTGGTCCTAATCGGCCGCGAAACCCTGCCCGACCGCGACGACT GGGACGCCTGGCTGAACCGCCCGCAACCGGTCGACGCCCACCACGAACGGCTGCTGCACAAGA TCCGCGCGATTCGCGATCTGGAAGCGCTAGGCGCCGAAGTCCTGGTCCTCGCCGCCGACGTCG 40 CCAACGAAGCCGCCATGCGCGAGGCCTACGATCGCGCCGAATCCCACTTCGGCACAATCCACG 25 GGGTGATTCACGGCGCCGGCCTGATGGACGCCCAAAGCTTCTCACTGATCGACGCCCTCGACC ACGACCTCTGCGCCCGCCAGTTCGAAGCAAAAATCCGCGGCGTCTGCGTGCTCGACCGCGTTC 45 TGGCCGACCGCACGTCGACTTCTGTCTGCTGATGTCTTCCATCTCCACCGTGCTCGGCGGCC TGGGCTATTTCGGTTACGCCGCGGCCAACGCCTTCCTCGACGCCTTCGCCCAGGCGCGCAGCC ${\tt GCGACGCCGCTTTCCCCTGGCTTAGCGTGGCCTGGAGCGATTGGAAGTACTGGACCGAGCGCA}$ 30

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AAGCCGTCACCCGCGTCTTGGCTTGGGGCAAGGCGCCCCACATCGCCCAACTCGCCCGGTGACC 10 CCGAGCCGGCTAGGCATGGACGTCCGGCGCTCTCCAGCGAATGGGTCGCGCCGCGCAACGTGG 5 15 ACAACTTCTTTGAGTTGCGCGGCGACTCGCTCAAGGCGGTCATGACCGCGGCCCGTATTCAAA AGGAGCTGAACGTGGAAGTGCCGCTGCCGACCTTCTTCCAGATGCCCACGGTCGCTGGCCTGG ${\tt CACATTACCCGCTCTCGGCCTGCCCAGGGCCGCCATTACCTGCACTACCGCATGGACCCGCGTT}$ 20 GTACCGCATACAACGATCCCTTCGCCAACCTGATCGAGGGTCCGCTGGACGTGGATCGCGTGG 10 AGCGCATCCTGCACCCTCATCCTACGCCACGACTGCTTCCGCACCTCGTTCCACTTCCGCG AGGGCGAGCCGGTCCAGGTGATTCACGATCGGGTGGACTTCAACCTGGCGCGGATTACCTGCG CGCCCGAGGATTTGCCCGAACGGATGCGCGATTTCATCCGCTCCTTCGATCTGGAGCGACCGC 25 $\tt CCGCCATGCGCGGCCTCTTCGTCACGGGGCCCGAGCGCCACGTGCTGCTAATCGATTTTC$ ACCACATTATCACCGATGGCGTGTCGTTCGAGAACTTCGTCGGCGAGTTCGCGGCGCTCTACC GCGGCGAGATCCTGCCCGAGCTGGAACTCGAGTACAAGGATTTCGCGGTGTGGCAGCATGAGA 30 ${\tt ACCGGGGCCGCGCCAACAGCGACCAGGCCCGCTACTGGACCGAGCAGTTGGCCAATGCGC}$ GCGTGCGGACCGTGCTTGATGCGGAGCTCGTTGCTCGACTCAAAGAGCACGCGGCGCGCCTCG 20 GCATCACCCTCTATAGCCTGCTGCGGGGGGATTCTCGTTATTGCAGCACAAGCTCTCCGACT 35 $\tt CGCACGACATCGTCATCGGTTCGCCCGTCGCGGGCCGCACCCGGAGCGAACTCCAGGATCTGC$ TGGGCGCGTTCGTCAACACCCTGCCGATGCGCCACCGCATCGACCCCATACCGCACGGG TCTTCTTGGAGCAGGTCCACCAGACAACCTTGGCGGCCCTCAGCTACCAGGAGCACCCTTTTG ACGAAATGGTGGCGACGCTCGGGTTCGCCGCCGATCCGGGCTCGCAACCCGATCTTCGACACGA 40 TGTTCTTGCTGCAGAACATGGCCATGGGTGCAACCACCATTCCCGGTCTGCGGCTCTCGCCTC 25 ACGACACTTTTCACCGCAAGGCATTGTGCGACCTGATGCTACAGGCGACCGAGTATGACTGCC ACCTGGAGCTGGTGCTCGAGTTCGCCACCGACCTGTTCCGGCTGGAAACCGCGCAAGTCTTGC 45 TCGACCGCTACCGCCAAGTCTTGGAGTGGCTGTTGGCGTACCCCCATGAATCGATAGACGATT TGACGCTCGCCGGCCACTTTCGCGAAGTCGAAGTGACGATGTCGGACGAGGGCGACTTTGATT TCTCAGATTTCGAACCCCGCAACGTGAGAAACCTATGGCGCGCCTGAGCCGCACAGATCTCCA

ACTCGCCATTCACCAGCGCACCGTGGAGCGCGAATATTGGCGCGCTCTGTTCGAGCGCCATCC GCAACGGTCCAGTTTGCCGGGGGTGCTCACCGCCCCGATCGGCGACGAGTCGACCCGCGAGAC 10 CTTGTCATTCGTCCTCGACGAAGATCCCCTTCGGCTGAGTAATCGTTCGCCGCAACGCCTGCT ${\tt CCTGGGGTTGGCCCTACCGCGCCAAGCCGATGACCATCACCCGATCCTCAACAGCTTGATCGC}$ 15 ATACCACGAGGCGATGCGCCACGCCAACTTTCCGCTGGCGACCTGGTGGCGCGGCCTACCCGG AGACCACGCGATCGGCGCTTGTTCCGGTTCGCATTGGAGGGTGAGCGCCTCACCTGCCGATT 20 GCGATTCGACCCTGCGCGCTATGACCGTCCCGCGATCGAAAACCTCGCCGATCGTTTCGCCCG 10 CTTCCTCACGCGCCTGTGCCGGGACGCCTCCACCGTCATCCAGGCGCTGGACCTTTCGCTGCC AAGCGATGAATCGGTGTGGCGCGTCACTGAAGGCGTGCGGCGGCGCTATTCGCAAGACCTGAC GCTAGACCGCGCGTTCCGCCGCCAGGCCGCGAAACGCCCGATCAGCCGGCGATCACGTTGAA 25 CGGGGACGTCCAGAGCTACGCCGAGGTCGACCGCCGCCACCTCCG 15 30 GGACCAGGCGCTGACCGTCACCGACCTGCCGCGGCTCTTCCTGGACGATGCCTCGCTCTTCGC TGACGGCGGGCTCGATGTGCCGCGCGGCGCCGACTCGCTCAATCCGGCCTATGTGATGTACAC ${\tt GTCCGGCTCGACCGGACAGCCCAAGGGTGTGGTGGTGGTCAATCGTTT}$ 20 35 GAATTGGGGGCAGTCCCGTTTCCCGCTGGACGAACGCGAACCGCAATCCTCCAAAAGACGCCGCT GCTGTTCGACGTGTCGGTCTACGAGCTGTTCTGGGGCGCATGGAGCGGGGCCACCCTGGACAT CCTCGAGCCCGGCGCGAGCGCGACCCCGACGCCCAGGGCCCTGGCCGAGCGCGCCAT TACCGTATGCCATTTCGTGCCTTCGATGCTGCTCGTCTACTTGGAAGTCATGCGGCGGCACCA 40 TGCGCCGCCGGGCCGGACCGGCTCCGTTACGTCTTCGTCAGTGGCGAGGCCCTCGAACCGGA 25 CCACCTCGCCGGGCTCCAGCAGATTGGTCGGCCGCCTCGGCCGCACGATTCCCCTCGTTAATCT GTATGGACCAACCGAGGCCTCGATCGAAGTCTCCTGCTTCGCCTGTCCCGCCGACCATGTGCC 45 CTACCTCAACCGTCCCGACCTGACCGCGCTCCACTTCGTGCCCAATCCCTTCGGCAACGGCGA

GCGCATGTACCACAGCGGCGACTTGGCGCTCGTGCGCGGCGACGGCCAAGTGGCGTTTCTCGG CCGCCGTGACCACCAAATCAAAATCCGTGGTCAACGGGTCGAACTGGGCGAAATCGAGAGTCA 10 TTTGCGCGGGCTCGAAGGCATCGCCGCCGCCGTCGTCCAGGCCGAGTCGCAGCACCATGAAAC CCTCGCTCAACATCTGCCCGAGTACATGATTCCCCAGCGCTTCTCGCGGCTGGCCGAGTTGCC 15 · GCTGCTGGCGGCAGGCAAGATCGACCGCCGCCCCTCGCGCAACGTGCAACGCCGCTCGCCAG CGGCGCCCTTCGTGGAACCCAGCGGGCCCACCCAGCAGCGTATCGCAGAACTGTGGCGCCA GGTCTTAGCGGTCGCCGAAGTCGGCGCCGAGGATCCCTTCTTCAGCATCGGCGGCAACTCGCT 20 10 CCTGTTCCAATACGACACCATCGCCGCCCAGGCCTCCTGGCTCGACGGGCAGGTTGACGAACG GGCCCAATCCGCCGCGCTCGACCGGCAGGCCGCCGAGGCGGCGCTGACCCTTCAAGAGACCGT GGCCATTTTTGAGGGATTCGATGACGAACCATGACCATCACGAGGAGAGCAGCGGCCTGGAGA TCGCCGTCATCAGCATGGCCTGCCGATTCCCGGGTGCTGCCGATTGCGACGCATTCTGGGAAA 25 TTGACGCGCGCGCCGCAGTACGTGCGCGGCCGGCCAGATCGATGACGCCGAAC GGTTCGACGCGGCCTTCTTTGGGTACTCCCAGCGTGAGGCCGAGCTGATGGACCCCCAGTTCC 30 GCCTGCTCCATGAATGCGCCTGGTCCTGTCTGGAACAGGCCGGCATCGATCCGCGCGTCGAAG TCGACCGGGGCTCGGCCGAATCGGAGCAATTCGCCGCCGAACAACTTTGCAACCGCGATTTTC ${\tt TGTGCACGCTGGTCGCCGCGCTCAACCTGAAAGGCCCCGCGGTGGTGGTTCAAAGCGCCT}$ 20 35 TGGCCTTGGCCGGTGGGGTGGCGCTGCGCTTCCCACGCCCGAGCGGTTATCGCTACGAACCTG GCATGATCTTCTCGCCCGACGGGGTGTGCCGGCCGTTCGACGGGGCGCTAACGGGACGGTGC $\tt CCGGCGAAGGCGCGGGGCTGGTAGCGTTGAAGACGTGCCCTCCAGGACGGCGACA$ 40 CGATCCACGCCGTGATTCGCGCGACCGCGGCAAACAACGATGGTGCCCGCAAGACCGGGTTCA 25 CCGCGCCCAGCGCCCACGGCCAAGCCGAAGTCATTCGCACGGCGCTGCGCCTGGCCCGGGTGC CGGCCGAATCGATCGACTACGTCGAGGCCCACGGAACCGGCACGCCGCTAGGCGACCCGATCG 45 AGGTAGCCGGCTTGGTGGAGGCCTTCGCCAGCGAGAAGCGCGGCTATTGCCGGCTGGGCTCGG TCAAATCCAACCTTGGTCATCTGGACACTGCTGCCGGCATCGCCGGCCTGATCAAGACCGTGC 3.0 TGGCGCTCGAGCACGCGCACATCCCCAAGTCCTGCCACGTCGCCACGCCCAACCCCGCGGCGC

GCCTACACAAGACGCCTTTCCGCATTGCCGCCGACGGGATGGCCTGGCCGCGCGTATGGCGA $\tt CGCCGCGGCGGCGGCGGTGAGTTCGTTCGGCATCGGCGCACCAACGTCCACGCGATTTTGG$ 10 ${\tt AGGAGGCGCCCCGCGCGCCCGAGCTGGCGGACGGGCGCAGTCAGGTGTTCGTCTTCTCCG}$ CCAAGGACGAGGCGCCTGGACCGTGCCCTTGCCAACTATGGTGCGGCCTTGGAGAAGCGCG GCGACCTCGCGGCGGGCGCGGTGGCCTGGACGCTCCAAAACGGCCGGGCCGCATTCGAATGGC 15 GCGCCGTCAAGAAAAACCGAATGGCGCGCGAGGATAAGCCGGTGGCGTTCTTATGTTCGGGGC AGGGGAGCCAGTACCGTGGCATGGGCCACGACCTGTACCGCGAAGAGCCGCGTTTCCGGCACC20 10 GGTCAGCCGCATCGAACCCAGCGGAGCTCCTCGACAGCACCGAATTCGCCCAACCTTTGCTTT TCTCCATGTCCTACGCGCTCGGTCGGCTGTGGCTCGACTGGGGCGTGCGACCCACGGCGATGA TCGGGCACAGCCTGGGCGAGTACAGTGCTGCATGTATTGCAGATTTCTATGCACTCGATCAGG 25 15 ${\tt CCGTCAGCGGTGACAGCGTTCTGATGCGCGAGCTGATCGCCGATGCGCTCGATTTGGCGGCGA}$ ${\tt TCAACGGCGCTGACCAATTTGTCTGGAGCGGGGCCGAGCCGAGGCTGTCCAAGCCGCGGGGGTCC}$ 30 GACTGCGCGGCCCGGCCTGCCTGCCACCGAGCTGAACACCTCACACGCGTTCCATTCAGCCA TGATGGATCCCATTCTGGAGGAGCTAACGGTTGCCGGTTCGCGACTTCAGGTCGGTGTCGGGA CGATTCCGGTCGTTTCATGCGTTACCGGAACCTGGTTGACGGCGAAGCAGCTGGCCGATCCGC 35 GGGAGGAGCCGCCGGTGATGCTCGAAGTGGGGCCGGGCTCGACCCTGGCGGCTTTGGCCCGCG AGCATTCGAATGCCCGCCTCCCGGTCGTCACCAGCCTGCGCCACGCTCGCCAGGCGACGCCCG ATCGCCAATACCTGCTCGAAACGCTCGGCTGCCTTTGGCGACACGGGGTTTCCGTCGATTGGG GGGCCCATGCCGGACGTTCGCGACGCTTGGTTTCGCTGCCCGGCTATCCCTTTTCCGGCGCGC 40 TGCGCCGCTTAGCCGGCGACCCCCTCCGCCTGCTGGCCGGAGCCCGCGCCGCCCCGT $\tt CGGGAACGCGCCGACGCGCGCGCGCGCGACCTCCCGAACACTCCGGAGCCGACATCCG$ ${\tt GCGCCGTGTCGGCGATCAAAGCGCCAATCGCCGGCCGATCCCGGCCTCTATCGCCTCTCCT}$ 45 GGCGCCAGGCCGGAACGGCGCCCGCTCGGTCCGCCCGATCTCGGTCCGCCCCGCGACTGGATCG TCTTCGCCTCTGATTCTCACCTGCTCCAGGCGCTCAGGGCCAATCTCGGGACGCGCGCTCAGC GGGTGACGCTGGTGACGCCGGGCCAGGAGTACGCAGCCGAGCCGTCCGGGTTTCGGCTGCGGC

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 $\tt CGGACCAGATCGACGATTACCGCGCCCTGTGGGGCGGACTTGGCGCAAACCGGTATTGTGCCAC$ GATACATCGCGTTCCTCGCCCCGTTCATGTACCGGGCGCGCATGCCGAGCCC 10 AAGCGACGCCCGGAATGGGCAATCCTGCACGGGATGGTCGCCGGCTTAAGCCGCGATTATC 15 ${\tt CCGAATGGCGCTTCGTCTCGATCGACGGCGGCGACCCATCCCCGCATCGGTGCGAAGGTCTGG}$ CCCGCTTGATCGCGCTTCATGCGGTCGACGAGGCTGGCCCGACCCGCTTGGCGCTGCGCGGCC TTCACGCTTGGGTTCCACAGTGCGAGCACGTTCAGCCGGCCACCATCCCTGGGGCGGGTATGT GGCGCGAGGGTGGTGTACATGATAACGGGCGGATTCGGCGGGATCGGTCTGGCGCTGGCCC 20 GCGCCCTGGCTCGAGAAGCTCGCGCCAAGCTGATCCTGGTCGGCCGAAACCTGCCCACCGCGC 3 C CGATCGATCTCGAGGCTTGGGACGCGCCGCCGTTGATTCTCACCGCCGACGTCGCCGACGAAG AGGCCATGCGCCGCGTCTTCGATGCCGCGCACGCCCGGTTCGGCGCCATCGACGGCATTCTTC 25 TGCTGCACGCCAAGGTTCGCGGTACCCTCGTGCTGCAAGGCCTGAGGGCAATCGATGCGCCGC 15 TGTTGCTGATGTCCTCGCTGGACGCCTGGCTTCCCGGTCCCGGTCAGACCGCCTATGCCGCCG CCAACGCCTTCCTCGACGCCTTCGCCAGTCTGCGCCGGCGAGAGGGGAGAGCCGGTGTACAGCG 30 CGCTCGCCCTCGACCCCCACCTGATGATCTCGCGCACCGACCTGACCTCGCGCTGGCACA GTCGATCCAGCCCTACGCCGGTCGCCTCGAGCGAACCCGAGGTGGCGCTGCCGCGCTGGACCG 35 CATCCGCCTGCCAAGCCGTCATCGAGCGTGTTTGGTGCGAGCACTTCGCCACCGCCGCCGTGC CTCCCGATGGCAACTTTTTCGAGCTCGGCGCCAGTTCCTTCGACATCGTCCAGCTCAGCGCTC GACTTCAACAACAGTTCGGCCGAGATGTCAGCCACACCGTGCTCTACAGTCATCCCACCGTCG CCTTGCTGGCCGGCTACTTCGCCAATGACCCGACGCCGTCCGGTGCTGCTGCCGACGAACGCG 40 ${\tt ACGAAGCGGTGCGTCGCGCCGACCTCTTGAAGAGCCGCCGGCGAGGAGTATGACCGTGGA}$ 25 CGTGGCCGCCTTCTGGCGCAACCTGGTCGAGGCCAAGGAGGAGCGTGCGCTTCTTCGAGGACCA 45 CGAGCTGCGGGCCGCCGGCGTGCCCGAGGAGATCTTGCGCCTGCCCAACTACGTGAAGGCCAA GCCACTGCTCGCTGATGGCGAAGCTTTCGACGCGGACTTCTTCGGGTTCCATCCGCGCGAGGC 30 CGCCTACCTGGACCCGCAAGTTCGGCTCCTGCACGAATGTTGTTGGACCGCGCTGGAGGATGC

 $\tt CGGCTACGATCCCGCGCGATCGCCTACCCGATCGGGTTGTTCGCGGGCGTCTCCAGCAATCT$ 10 TTCGATTCAAACCGCCTGTTCGACGTCACTGGTGGCGATTCACCTGGCGGCGCAAAGCCTGAT CGGCGGCGAGTGCCACATGGCCTTGGCCGGCGGAGCGACCTTGGAGGTCCCCAAAAAGCCCGG 15 CTATCTCTACCGCGAAGGCTACATCAACTCGCCGGACGGCCACTGCCGGGCCTTCGACGCCGA CCTACGCGACGGCGATCACGTGTACGCAGTGATCAAAGGCTCGGCGATCAACAGTGACGGCCA TCGCAAGGTGTCCTACACGGCGCCGGGCAAGAGCGGTCAAGTGGCGGTGATCCGCGCTGCGCT 20 10 ${\tt GGCGGCGCCAGGTAGAGCCGCAAACCATTCGCTTCGTCGAGGCCCACGGGACCGGCACACT}$ TTTCATCAAGGCGGTCTTGGCGCTCGAGCGGCGCGTCCTCCCGCCCAGCCTTCACTTCGTCCG 25 GCCCAACCCGGCCATCGATTTCAACGGGCCCTTCTACGTTTGTCGCCAAATCGAGCGGTTGAC GGAGAACGGGCGGTTGCGGGCCGGGGTGAGTTCCTTTGGCATTGGCGGCACCAATGCCCACGT 15 30 TCCGTTCCTGTTCCCGCTATCGGCCAAGACGCCGGATGCGCTGGCAGGCCGTTGCCACGACCT TGCCGACCACCTGCGGGCGCACCCCGAGCTCCTCCTGGCCGATGTGGCCCTCACTCTGCAGAT GGGGCGGGCGTCGTTCGCCTACCGCCATGTGGTCCAGGCTGCGACGGCGGAGGAGCTGATTCG 20 CGGTCTGGGAGCGTTCCGACAGGAGTCCATCCGCAAGAGGCGGAATCGAGTACAATGGGTGTT 35 GGCAGGCGAGGCGATGTCGCTTGACGCCGGTTTGCGGCTGTACGCCGATTGGCCGGTCTATCG GGAGCGGGTCGACGTCTGGCGATCGTCGCCAAGCTGCGCCAAATCGACGGCCGGTCATT ${\tt CCTACATGAGTGGATCGAGCGACCGCGCGAGGTTCCTGCCGAATGGTCGACGGCGCTGGCGTT}$ 40 GAGCCGTGGGCTGGGCGGACAGGTCGGCGTGGTTTTGGCCGAATCCCTGTCGTTGGAACAAGC 25 GCTGGCGCTGGTGTTGTGCCAGACACCGGTTCCCGGCGATGCCACACCTCAGCGCGAACGCTT GGTTCGGACACTGGAAGGCTGCCGGTTTCGTCCACCACGATTTTTGATTTCGGCAGACAGCTC 45 GGGTCGACCCCTGGACCTCGCCGAATTCGCTCATGTCGATTTTTGGTGCGGTGGCCAAAGCGC CTCGCCCAATGAGGCGGAGCTGCGCTCATGGAGCGACGCCGCGCCCGAGCTGGTGACCTTGGC GATCGGCCCATCCTTTCTCGAGGCCGCCCTCCGGGACGGTGGGTCTGGCGATCGACCCCAAGCG

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10 AATTCCCACGATCGGCGACCCCTTCGCGGAGCAGGCGGGGGGGAGGATGACTTGATTGCGGCGAG $\tt CGCTTCCGCGTCGGCCGGATCGCCGCCGAGCCGTCGGCAAACTCGGCAGCGGAACGCCCACG$ CGCCCAGTCAAGCATCGCCTCGGCAACCACCCGGCTCCGTCTCATACGTCGGCCAGCGTGGC CGTGGCCACCATTCTCGAAACCGTCCGTGCCTATTTCGGGTTCGCCGCCGTGCGTTCCACCGA 15 CGCCTTCTTCGAATTGGGCGCGTCCTCGCTGGATTTGGTCAACCTGGGCCAGCTCCTTTCCGA TCGTCTCGGCCGCGAGGTTCCGACCCTGCTCCTCTACGACCACCCCAACACCCGGACCAGTTGGC GCTGGCCCTGACATCCGCGGCGCTCAGCGCAGAGGCGCCCCCTTAAGGGGCGGTCATCGCGC 20 10 ATCGACTTCCGGCACAGCCGCGCGCCTCCACCGCACCGTTCCCGGGGGACGC ACCGGGCGCCGACGACCTGGACGCGTTCTGGAACAACCTGGTCGAAGGGGTCGAGTCGATCAC 25 $\tt CTACGTGCGGGCCAAGGGGGAACTGACTGGGATGATGGATTTCGAACCGGAATTTTTCGGTTA$ 15 $\tt CGCACTGGAGCACGGGGGCTACGATCCGACCCGATGGGGGCATCGATTGGCGTCTACGCCGG$ CGTGACCAACCACCTGCCTTGGCTGATGCGAACTTTGCCGCACCTGACCGAGGAGGAGCAATT 30 $\tt CGGCGCGCTGCTCCTCACCGACCGCGAGTTTTTCGCACCGCTGCTCTCCTACAAGGTCGGCCT$ GCGCGGACCCGCTATTTCGCTGCAAACCGCCTGTTCGACGTCGTTGGTGGCGATCGGCACGGC 20 35 CGAGCGCTGCGGCTACTTCCACCAAGAAGGCTACATCCTCTCGCCTGACGGCCACACGCGCAG CTTCGACGCGGCGGCGCCGGCACGGTCTTCGGCGACGGAGTCGGCATGGTGCTGCTGAAGCC GCTGGCCCAAGCCTTGGCCGACGGCGACACGATCCACGCGGTGATCAAGGGAATCGGCATCAA CAACGACGGCGCGCAAGGTCGGCTTCACCGCACCTAGCCGGGCCGGTCAGACCGAGGCGAT 40 ${\tt TCGGGCCGCGCGCGCGGGGTGGCGTCGAACCGCGTCAGCTACGTGGAGGCGCATGG}$ 25 AGCCGACGGTCCGCTTCCGCCCGGCTCCTGCCTACTCGGCTCGGTGAAGTCCAACGTGGGCCA 45 ${\tt CCTSCCGACCAGCCTGTTCTACCAGTCGCCCAATCCACATCGACTTTGCGGCGAGTCCGTT}$ ${\tt CCG2GTGAACGGCCAGACTTCGGATTGGGTCGCGCCAGAGGGGACGCGGTTGCTGGCGGGAGT}$ 30

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ACCGACGACAGCGGCACCTCTGTCGACGGAGCCGAATGACCTCGACGGGGCGACGCCGACGG
GCTAGTGCTGCCGATCTCGGCCCGCACGCCGACCGCCCTGGCGCACATCGCGACCAACCTCGC
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TGTCTCGATCACCGTCGTCACCGCCGGGGGTCGTCGCCGTCGCGGACGAAGCGATTCGCGAGCC ${\tt GCTGCAGGCGCTGATCGTGGCCCGTGCCTGGTCATCCCGCAGGAGTTTCCCGGGCTCAGCGT}$ 10 GCTCTCGGGCACGGATCACATGGTGGCGCTGCGCGGCGGCGAGCGCCTAGTGGCCGATGTCGA ${\tt TCAAGTCGATGGCCTCGGTGTGGGGGATCGCCAAGGTGCCCTTGCGCCGCGAGGGCCACTACCT}$ 15 GATTCTCGGCGGCCTGGGCGATATCGGCTACCACTGTGCCCGCTATCTGGCCCAAACCTACCG GCGCGAGGGAAACCTGGATTCCCGGCAGCGCACGCGCATCGAGCGCGTGTTGTCGCTAGAGGC $\tt GTGCGGGGCCGAAGTCCAGACGGCTGCGGTCGACTTGGCCGATCGCCATCGCTTGGCCGATGT$ 20 10 GGGACACGTCCACTCGATCGACGAGCTGGTGCGCGTCCGCGACGAAGCCCAATTCACCGCGAA ${\tt GGTTCGAGGGCTGCACCTGGCCGAGGTCGTCGATCCGCTGAACCTCGACTTTTGTCTGCT}$ GTTCTCCTCGCTCTCGACCGTCCTCGGCGGGCTCGGCTACGGCGCCTATGCAGCGGCCAACGC 25 15 GATCGTGCCCGAGGACGCTCCGGCCCTGTTCGCGCGGGTGCTAGAGCGACTTCCGCAATCGTT 30 CATCGTGTCCACCGCGACCTTCGGGCCCGCATCGACACTTGGATCCGGGACAAGAACCGCGT CCCGCCGGCGAGATCCGAGCGGTTCAACCGCGACCGGACCTGAGCCAGGCGTACGCCCCGCC GATCGGCCCGCTGGAGATTCAACTCTGCGGGCTGGTCTCCGCCTATTGCCGGTTCGACCGGAT 20 $\tt CGGGCGGGACGATTCCTTCTTCGAAATCGGCCTCAGCTCGACTTGATCCAGCTCAGCTC$ 35 GCGCATTCACCGCATCACCGGCAAGGATCTCAATACGACCCAACTGTTCAGCTACCCCACCGT ${\tt GCGCGCCTTGGCGCTCTTCCTCGGCGGCGAACCGGAGGGGCCTCGCGGCGAGGAGCCCGCCAT}$ GCGGCGCTACCGACCGCGGTCGAGGATTTTCCGCGCAGCGATCCGGGACGACTCGCTGAAGAA 40 GCGCGATAGAAGAACGGAATCGTGTATGAAATACGAAACCACCGGATTGGAATTGGCCGTCAT · CGGTCTCGCTTGCCGCTTTCCAGGCTCACCCGATCCCGAACAGTTCTGGTCGAATCTGCGCGC AGGTCGCTCCGGAATCCGCCATTTCAGCGATGCCGAGCTGAGCCACATCCCCGCATCCCTGCG 45 TCACCATCCGCATTACGTCAAGGCCAAAGGCGCGCTGGACCACGCCGATTTCGAACCAGCCTT CTTCGGCTACTCGCCCAAAGAGGCCGAGGTGATGGACCCTCAATTCCGGCTGCTCCATGAGTG $\tt CTGCTGGGAGCGCTGGAGTCAGGCGGCTATGCGCCGAGCCAATTCGCGGGTCGGATCGGCTT$

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GTTCGCGGCGGCGGCCTTCAACGACGGATGGATCGCCGGTACCCTCGACCGGCTGCGCACCGG ${\tt CGTGGGTTTGAGCTCCTGGAAACCGCGTTCTTGACCCTGCGCGATTACCTGACCACCCAGAT}$ 10 15 GCGCGACGGCGTCTGCCGACCGTTCGACGAGGCAGGCGCCGGTACGGTCTTCGGCGACGGGTG CGGCATGGTCCTGCTCAAGCGGCTGAGCGACGCCCAGCGCGACGCCGATACGATCTGGGCCGGT CATTCGCGGGGCGGGCGTGAACAACGACGGCACCACAAGGTTGGCTACACGGCTCCTGGCAC GAGGGGCCAGGTGGCTTTGCTTAAAAGTGTTTATCGCGCGAGCCGGGTCGACCCGGCGACGCT 20 1.0 TACCCAGGCCTTCGCCAGCAAACGTCGCGGCACCTGCGGCTTGGGCTCGAAGGGCAACCT GGGTCACCTCAACACGGCGGCCGGCATCGCTGGACTGATCAAGGTGGTGCTGGCGCTGAAACA TCGCGAAGTGCCACCCACCCTCAATCTGCGCCGTCCCAATCCGAAAATCCGCTTCGACGAGAC 25 GCCGTTTTTCCCAGTCGTCGAGTTGCAACCCTGGCCAAGCGGGACCGGCCCCTTGCGAGCCGG 15 GGCCAACCCGGCGCCACACGGCAGATTCCGACTGTTGCCGCTTTCGGCCAAGACACCGGCTGC 30 GCTCGAAGCGAAGCGCCGGATCTGGCCGGCTTCCTCGAACGCCACCCGGAGACCTCCTTGGC GGAGACCTTAACGTCCGCGCGCACGCGGCTGAGCGGCGAGTCGTCGAGCACTTGCGTGGTGGG 20 35 CGGTCTGTATCACCATTTCGAGCCGTTCCGCACGGCCGTCGATGCCTGTCTGCGCGAGCTGGA TTCGACGACCTTCGTCCAACCCTTGTTGTTCCTCGTCGAGTACGGGGTGACCGAGTGGCTACG CTGCTTGGGTGTGCGGCCAACAATGGTGTTGGGTCACAGCTCTGGCGAGTATGCCGCAGCCTG 40 GCGCGACCTGCCAGCCGGCGCCATGCTCGGCGTCCCGCTGGCCGCCGAGGCGCTCGAGGCGAT GTTGCCCGACGCTCTCGATCTGGCGGCGATCAACGGCTGTCAGCTTTGCGCCGTGTCCGGGCC 45 GCACACCGATCGCGCCTTCCACTCGCGGCTGGTAGCACCGGTGCTTGACCGGTTCCAGGCAGC $\tt CGTTCAACACGTGGAGCTGCGGCGGCCGCAAGTACCTTACCTCTCGACCGTCAGCGGGCGATT$

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GGAGGCGGATGGGCCGGCGAACCCGCACTACTGGGTGCGTCACCTGCGCGACACGGTGCGGTT TGGTCCAGCCCTGGAGGCGCTGCCGCCGGTGGATTCCTTCGTGTGCATCGAGGTGGGACCAGG $\tt CTCGGCCTTGAGCACCATGGCGCGCGAAACGTTGGGTTCCCAGGCGCGACTGATTTCGTTGCT$ GCCGCGGCCGAACGGGGCAAATCGAGCCCGGTCCGGTATTCGAACGACTGGCGGCGCTTTG GCGCAGCGGGTTGACATTGGATTGGTCTAAATTGACGGGCGGAAGAGGGTCATCGAATTCC ${\tt TTCGTCGCGGCCTGCAGTCGAATCAGGCGCCATCCTTGCCGAGCGATCCGCAGGGGAAAACGC}$ ACTCGAGGCTACCGACGCCGCGGGTACTCGCGAGCGGCGAGCTTGGCGAGCTTGCT CACGCGGCTGCGCCCTGATTCACCAGCGGTTCGATGTCGATCTCGGGCTCGACGAAATCTT CTCCATTCCCAGCGCCGGACCAGGACGACTATCCCTTGTCATCCGCCCAGCAGCGGATTCA CAGCATCGTCACGAGGGCCGAGGTCGGCACTGCTTATAATTTTCCGATCGTCCTCGAGCTGCA 15 GGGCGCTCTGGATCGAGTGCGATTCGAGGCGACGTTCGCGGCATTGTTCCGGCGTCATGAGGG GTTCCGCACCCGCTTTGTGATGCGCGATGGCGGGCCGCCCAGCGCATTGTACCGGACGTGGC GTTTCGCCTGCCGCTCACCCAGGTCGAGCCAGAGCAGGTTCCCGGGCGCATCGAGGCCTTCAT CCGTCCCTTCGATTTGGAACGCGCGCCGCTGTTCCGCGCGGAGCTGTTGCAGTTGGCCGAGCA GCGCCATCTGCTACTTTTCGACATGCACAACTTAATTGCCGACGGTATCTCGCTCAACCTGTT CGTCGCCGATTTCGCGGCCCTGTACCATGGTCGTCCGCTGGCGCCGCTGAAACTCCGCTATCG ${\tt GGCGGTGCGCCGTACAAGGGCCGTAATGTGGTGTTCCACCTGGACCGGGAGATCCGCGACCG}$ ${\tt GCCGCACAGCGAGCTGCATCCCGTGATCGGGCTCTTCACCAACTTTTTGCCCTTGCGGTTGGC}$ GGTCGAGGGATCGACCGCTTCGATCGCTTCCTTGCCGCTTGCCACCAGGTGTTTCTCGAAGC GTCGCGGTCGCCGCTGTTCCAGACCTCGCTCGTCTACCACAACGAAATTGACGGCAAGACCAA

TTTGAAGCTGGATGTGACACCTTTTTCCGACCGACTCGAATGTGTTTTGCAATACGACTTGGA TCTGTTCTGCGAGGAGACGATGCGCGGCCTGATCGCGGGGTTCCAGGCGTTGGTGGCGGGGGCT TGTCGCCGATCCGGCGCAATCGCTCGCCGCCGCGGGCGTTTCCGGGAAGCGGGCGCTGCGCGC GGGCGTGGCCACGGCAAGCGAATCGTCGCCGCAGTCACTGCCGCCGCAACCATCGACGGCGTA GATCTTGGCGGCCTACGTGGGGCAGAACCCCCATCCGTTCGCGATCCATCGGGGTCTCATTTT ${\tt CCTGGTGCGGCTCGACGACCTGCGCGGGTTGGTCAATCCTCAGGCGAATGCCTTCACCCTGGC}$ 10 GTCGGCTCCATCGCGCTGGTTGCTATTGCTGACGGTTCATCCATTGATCGGCGACAACGGCAC GGTCGACCTCTTTCTGGCGGCACTCGCCGATCACCTGCGCCGCGCGCCCCCCTTTTCCCGTAGC GCTGACCGCGATCGCGCCGGTCCTGGGCCAATTGCGCGAAAGTCGGCTGAGTCCTGTGGCCCA 15 GATGTGGCTGGACGACGTCTGTCGCCGCCACGACCTCACCCCGCTAGAGGTCTTGGCGGCCCG GCTCCTCGATTGGACACGAAGCCACGGTCACGGGTCGATCGCTTTGTGGACGCCGCTGCCCGA GCAGCGAGGAGCGGGCGATCCAAGCTGGCTCGAGCAAATCGCCTTGAGACGGGGTACCCCTGC ${\tt AACGGAGGTCGTTTGCCCTACTCCGACCCAACGGGCAGCCATCGACCTCGCGCTGGCCTGGCT}$ ${\tt GCCGCAGCCGCTCTTCACGGTTTGGTCGGAACCGTTCAGCCGGGAATCTCCATTGGT}$ 20 CTGTCCGTTTCCCCTCAATCTCGCGTTCCGGCCAAGCCATCCAATTGCCTACGCGCTCAAGCA CGAGGCCACGCTCGCGGTCACGGCACGGGCGCGCGATCTGATGCGTTTCCTCGACGGCTTGGG CCCGGAAAGCTGAAGATTAGCATAAGCGCCCGGCCAAGGGCATCCTAGGATGACGCAAGCCTC GGCCGCGTCGACGTCCCAGGTCGCCGGAGGTCACCCCCGGCCGAAAGGACGACGATGACGA 25 TGGGCGGCGATGAAGCGGGGCCGGACGCCGGAGCAGGCCGGCGTGAAGCTGCTCCGCGCCC AGGTGTGGGCAGGCTACCGCGCGAGCGCGGGATGACCCGAGCCCCGCCGGCGCGACCAT 30

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10 $\tt CTCGGCGACTACGCCGGCCGGACGTGGTCGCCGCTTCCGGCAGGAGGCGATCGCCGTC$ AACATCATCAACCACCCGGGAATCGTCCGCGTCTTCGACTCCGGCGAGCTCGAGGACGGCTCG 15 GAGCTCGCGCCCGGGGGCAGCCGCGTCAAGATCCTCGATTTCGGCATCGCGAAGGTCCTCTGG 20 10 AGCCCGCTGGGCGCGAGCGCCACGCCAGAGAGCGCCCTGGGCGCGAGCGCCACGCCAGAGAGC GCCCTGGGCGCGAGCGCCACGAGAGAGCGAGGCCCACGAGGAAGACGCGCTCCGGAGCCTC CCCGTCGTGACCAGCGGCAGGCCCGCGATCCACCCGGGCGGTCGAGATCCCGGCCGAGGCG 25 15 AGGAGCTACATGGCGCCGGAGCAGGAGCGCCACTCCGGGAGCGTGGACGTGAAGGCGGATGTC30 TACTCGCTCGGCGTCATCCTCTATGAGCTGCTCGAGGGGCGGACGCCCGACGCGCCGAGCGCC GCGTGGCCGCCCGATGAGCGCCGCCACGCCGGTCTCGTCGCCCTCGTCCACCGGGTT GGCCGGGCGAAGAAGGAGCTCGACGAGGCGCTCTCGAGGTGGGTCGTCGGCGGAGGGGCGCCCG 20 35 GGGCTCTTGCCGTGCGGCTATGCTCTTCTCGAACTGGTCCTCCTGGGCCCTGGGAACTTATAC GATTCTTTCCAGCCTGTAAGTGCATTTTTCTTTCAATATCGTCCTCTCTTCATATACGAGGTG AGTTCTCTGAGGTCCTCCTATAAGTCTGGGGTGTCCTATTCGGCCTCTTACTTGTTACTTCGC 40 TATCTCATTCGCTAATACGTTTCTGTATTGTGTACATCTCCTATCATGTGTCAATACTTGTTT GATTATCGCACTTGAATTCGCG

or its complementary strand,

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(b) DNA-sequences which hybridise under stringent conditions to regions of DNA-sequences according to (a) encoding proteins or to fragments of said DNA-sequences,

- 5 (c) DNA-sequences which hybridise to the DNA-sequences according to (a) and (b) because of a degeneration of the genetic code,
- (d) allele variations and mutants resulting by substitution,

 10 insertion or deletion of nucleotides or inversion of nucleotide segments of DNA-sequences according to (a) to (c), wherein the variations and mutants offer isofunctional expression products.
 - DNA sequence according to claim 6 selected from the fol lowing
- 30 (a) open reading frames:

			Nucle	otio	de Position				
35	20	ORF1	1666	-	1	Seq	ID	No	3
33		ORF2	1605	-	3338	Seq	ID	No	4
		ORF3	6100	-	3398	Seq	ID	No	5
		ORF4	7110	-	6374	Seq	ID	No	6
40		ORF5	9590	-	8433	Seq	ID	No	7
	25	ORF6	11393	-	9855	Seq	ID	No	8
	•	ORF7	13656	-	12712	Seq	ID	No	9
		ORF8	15374	- .	18984	Seq	ID	No	10
45		ORF9	20003	-	27889	Seq	ID	No	11
		ORF10	28251	-	29402	Seq	ID	No	12
	30	ORF11	31720	-	30401	Seq	ID	No	13

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		ORF12	31982	-	32932	Seq	ID	No	14
10		ORF13	33128	-	33613	Seq	ID	No	15
		ORF14	33661	-	34007	Seq	ID	No	16
		ORF15	35611	-	35255	Seq	ID	No	17
	5	ORF16	37856	_	35730	Seq	ID	No	18

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or DNA sequences complementary to said open reading frames,

- (b) DNA-sequences which hybridise under stringent conditions
 to regions of DNA sequences according to (a) encoding proteins
 or to fragments of said DNA sequences,
- (c) DNA-sequences which hybridise to the DNA-sequences according to (a) and (b) because of a degeneration of the genetic code,
- (d) allele variations and mutants resulting by substitution, insertion or deletion of nucleotides or inversion of nucleotide segments of DNA-sequences according to (a) to (c), wherein the variations and mutants offer isofunctional expression products,
 - and peptide sequences corresponding to said open reading frames
- SEQ ID No 19 (>ORF1)
 - VDPEREAVTLGLAFNRAQGRTYARGPEARAEYIGTAMRAADVIEDRFEIERLAVSGGMGDVYR ARDRVSGQAVALKVLQGASANDLRRFAREAEALVTLRLPGVVQYVAHGVTGAGRPYLAMEWLD GVTLEERLAGAPLTLAESVALAARVATTLGAIHWLGVVHRDLKPSNLMLVGGAVERVTLLDFG IARHLRLAPTLTSPGAVLGTPGYIAPEQVRGDAPVDARDVFALGCVLFQCLAGRPPFLGNSAL ALLMRVVLEEPPRLGELRDGIPEPLERLVARMLAKNAGERPRDGAAAAAELAAVAGEGLSIGA SAVAAPAAPGEAITTAERKVMCVILAEDGGAEAGATLSEDDGAARAEALRDIAARHGGRLDRL

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QARWWLVALSGAESPTDLATRAAHCALALRAALGGVPVSVATGLAEVEARLPVGELVDRVAQL IAGRDGI.SPPEIRLDDATASLLASRFETVQGPGGCWLRGPKEEPDAVPRLLGKPTPCVGRERE LSQLATEWRHCVDEPSANAVVVVGAPGLGKSRLAWEFLRTLEOREGAAI

5 SEQ ID No 20 . (>ORF2)

VRPCARLNASPSVTASRSGSTAAGSVHASTSACVEQPATGRTQPASPRWPPGAAALRLTSAMP
RWFNTAGPCNPADHYMLPAEERLPAVRDLVDRKAYFVLHAPRQIGKTTSLRTLAQDLTAEGRY
VAVLVSAEVGAPFSDDPGAAELAMLAEWRGTAGAQLPADLRPPPFPDAPAGQRIGAALRAWAQ
AAPRPLVVFLDEADALRDATLVSLLRQIRSGYPDRPRDFPHALALVGLRDVRDYKVASVDSGR
LGTSSPFNIKVESLTLRNFTRDEVATLYAQHTAETGQVFRPDAVDRAFELTQGQPWLANALAR
QLVEVLVKDRAQPITSANVDRAKEILIERQDTHLDSLVDRLREPRIRAVIEPMLAGTALPSVP
PDDLRFAIDLGLVRMTAEGGLDVANPIYREIIVRELAFPIRASLPQIKATWLTQDGRLDADRL
LDAFLSFWRQHGEPLLGAAPYHEIAPHLVVMAFLHRVVNGGGTVEREYAIGRGRMDLCVRYAG
ETLAIELKVWRDGRPDPVAEGLAQLDEYLAGLGLDRGWLILFDQRSGQPPIAERTRRERALSP

15 AGREVAVIRA

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30 SEQ ID No 21 (>ORF3)

HIGHVFSYTHTDVVVRQRRMRGFNIFYPMGWDDNGLPTERRVQNYFHVRTDVRTPYERGLTLP
QAAPETIKKEPPRIVSRPNFIELCHKVTREDEQVFKALFRRVGLSVDWRNEYATIDDHCRRTA
QLSFLDLHEKGHLYSVFAPTMWDVDFQTAVAQAEVEDRPQSGAFHDIAFAVEGTAEELVIATT
RPELLAACVGVTAHPEDPRYQHLFGKTALTPIFRAPVPIFPSPLVDREKGTGILMVCTFGDAT
DVIWWREQKLPLRQMLGKNGRVLPVTFGEGAWESRDPAAANAAYAPLQGRGVKQARAAVVELL
RREEHAAAPGRGPALRGEPRPIERAVKFYERGDQPLEFVPTRQWFVRLADKKAELLEYGDKIK
WHPDFMRLRYRNWTEGLQGDWCISRQRYFGVQFPVWYPLDAEGNPDHSRPLLATREMLPVDPT
VDVPPGYEASQRDQPGGFTAESDVFDTWFTSSLTPQISSHWGDDPARHARLFPADLRPQAHDI
IRTWAFYTIAKAMLHESSVPWHHVAISGWILDPDRKKMSKSKGNVVTPMHLLDTYSSDAVRYW
SASARLGTDTAFDEKVLKIGKRLVTKIWNASKYVLSQSAEVHPISEELDRALLHKLSAVVDDA
TRSFDEHEFAAALERTEDFFWRWFTDAYLELAKARARGEGGAGEAARGSAVAALRLGLSVLLR

 ${\tt LFAPVLPYITDEVWRWVYAEETGDTSIHRAKWPSAADFAAVAAPSDPGLLDLAAAAMAAVNKR}$

VTIKKTFRSIDPATLPKHFDSPVAELRLADLWEADGTYRYDPSRPREETFVVDTPPPTASGSL

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KSELGASVGRVVTDLALGANAATLARLKPALGDVLTAVRAGAHALVRPELADGEVLVVRCELE PAAAAAAGAGGAAASEE

SEQ ID No 22 (>ORF4)

- 5 MIHAEPFEARLVAARPLSPFVRELSFERADGRSFLFEAGQWVNLVLPLPGGEVKRAYSIASAP
 DGSPRFDLAVTLVQGGAGSEHLHRIEPGATLRAIGPHGLFTRDPGDSAPSLFVATGTGITPLR
 SMLRASLRAGLAAPHLWILFGARFEEDVIYRDELEALARGSDRIRYEITLSRGGPSWAGRRGY
 VQAHVPELYRELAEKSGDPAPHVFICGLDRMVSSVRELARGELGVHRKHVHVERYD
- 20
 10 SEQ ID No 23 (>ORF5)

 MKSLPSDRAARLAQSDIRTMTLACA; KVHGINMSQGVCDTPVPSVILQAVKEAMDRGCNTYSRF

 DGIVELRHAIAAKLARHNGIAADPETDITVSAGATGAFQATCMALLNPGDEVLLFEPFYAYHA

 25 QAILAVEAVPRYVTARSLSWNVDGDELERAITPKTKAIVVNSPGNPSGKVFGRMELEQIADLA

 CHHDLMVITDEIYEYFIFDGREHVSVASLPRMSERTITIGGYSKTFSITGWRIGYSVADARWA

 15 KAIGAMSDLLYVCAPTPLQHGVAAGIRGLPRSFYTGLAQGYERKRDRFCRALEKAGLPPCVPQ

 GTYYVLADVSRLPGRTGRERAIYLLDETGVAGVPGDAFFEGTQGSRFMRFCFAKTDEDLEEAC

 ORIEOLA

SEQ ID No 24 (>ORF6)

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VSDPRKERLGDMDLEEFRRIGMRIIDWAADYLGHPDRYPVFPAIRPGDVKGRLAPTPPVEPEP

MDAVLTDFEQIILPGITHWNHPRFFAYFANTASGPGILGELLAACLNVNVMLWRTSPAATELE

ELVLSWLRQMLDLDAGLHGAIMDTASTASMVAIAAARDSAEPTIRLRGMAGQRRMRLYASEQA

HSSIEKAAITLGIGQEGVRKIPTDFAFRMVPEALRAAVVEDLGAGLRPFCVAATVGTTSTTSV

DPIPAIVSVCREHGLWLHVDAAYAGMAAIVPEHRDVLAGCEGADSLVVNPHKWLFTPMDCSVL

25 YVRDADRLKRAFSLVPEYLRTEGDVTNYMDWGIQLGRRFRALKLWMIVRYFGHEGLAARIREH

LRLGQQLAQWVDADPDWERLAPTPFSTVCFRMRPSALACIMRSADEAERESIERELDRLNEAL

LDEVNKSGRVFLSHTRLHGRYTIRVAIGNIRSDEVAVREAWECLRAAGARLCADERFVSCSRS

ADEGRGKS

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SEQ ID No 25 (>ORF7)

MRREEPVLEAFYERYCAAPRETSYHVELPVDVELHQEAAPALPQARSLELAGRVALVTGSSRG IGKAIALRLAEQGADVAVNYHSNKDAAEQTAAEIRALGRRTMVVQADVTRPNAAAELFSSVEA QLGPIDILVNNVGDFFFKPLAAMTDDEWRNVMDSNLSSVHYLCRAAVARMRQRKSGRIINIGL SPTYAIRGAPNVAAYSIAKTGVLILTRSLATEEAPHGILVNCVSPGLIDNGYLPPAQKEWMER RVPMGRLGRASEVADAVAFLASDRASYVSGANIAVAGGWDWTDRGTEHDRRVDLFIGHEEP

SEQ ID No 26 (>ORF8) MSGRFPGARNVEELWQKLRAGVECVVTFTEAEALAAGVSREMLANPSYVRRGAPLDGVELFDA SFFGFSPREAESMDPQQRIFLEVAWEALERAGYDPDAHSGPIGVFAGSAPSGYHSLAQSDPEI. ${\tt LGALGHYQLTLNNDKDYLTTHASYKLNLRGPSVCVQTSCSTSLVAVV{MACQSLLNHECDMALA}}$ GGVG1HAHQRRGYLYQENG1SSPDGHCRAFDVAAKGTVGGSG1G1VVLKRLADALADGDHVHA VIRGAAINNDGSSKIGYTAPSVQGQAEVIGMAQALAGVEPDDISYIEAHGTGTPLGDPIEIAA LTRVFRAKTARRQFCAIGSLKTNLGHLDAAAGVASLIKTVMALEHRELPPSLHFERPNPKLEL ESSPFYVNTRLTPWHAARGPRRAGVSSFGIGGTNAHVVLEEAPAPPPSGPSRRWQLLTLAARS EAGLARATADMIEHLDRHSGTSIADVTYTSHVGRRAWPFRRAVVGESAADLRAALASEGSPRS ISSCQAARERPVVFLFPGQGAQHLFMARELYEVEPIFRQSLDRCAELLRGPLGLDLRQVLYPA EGQRDDAEQELGRTAIAQPALFAIELSLAKLWMAWGIVPQAMIGHSVGEFAAACLAGIFREED ALRLVAERGRLMQQMPPGAMLAVPLAEPELAPYLSDDISLAAINGPALSVVAGPIEAIDALAA ELLDHGLSCRRLHTRHAFHSKMMAPVVDAFTRCVSAVERRPPSGHFLSTLTGGWISPEAATIP AYWARQLVEPVRFAQAVRQLLSESTWLWLELGPGQTLSPLVRQQARADGGQVVVASLPRAKDA GADHLAVIEALGRVWSAGGTVDWKRFHEGEARRRVLLPTYPFERQRYWASPRHTSAPPEAIIK PLLAKNPNVADWFFLPAWRRSDPPVSFDAQAVTTRRSTWLVFIGDEGLGAALVEGLARRGHEV VAVVTGERFEQTGTQRYTIDPAANGDVASLFARLEIEGRMPDRIVHAFCTSPADGARIERGAA LEIERRLGFDSLLLLAQVIAAQRHPKPLMLGVITTRAHSVIGTEIIEPLRALVLGPCRVIPQE IPHVSCRNIDIDLPGEGGRAEIAARLIADLERESPDSVVAYRGGRRWVESIELTDVGRRSAGA APRLRQRGAYLITGGLGGIGLVAAELLAREAHARLILVGRTGLPARQGWDDWLAAHGAGDATS

RKILRIRALEEAGAEVKIAAADVSDFNAMRSVIEEARTRFGRIDGVIHSAGIASGGMIQLRTP MAAWRVMAPKVGGTLVLDALLRDERPDFLLICSSLASLVGGATQIDYCAANAFLDAYAQSREG EEGCRVISYQWDTWSDVGMAVDFKLPADLQEGRRESLKRGISSSEGAEVLGRILSAGMSGPLA

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ICTSDLPAYKQSVTTRRSQHEQTPAARPMHSRPTTTGAYVAPETETERRIAAIWQDLLGLEQV GANDDFLQLGGHSLLATQVLSRVLQTLKVGISLPQFFDAPTVAGLSRLVDAARAEGAGPVAPA IGRVERDAYRIKPPAAEQAARTKP

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5 SEQ ID No 27 (>ORF9)

MEPVGGVDMNQPAKQQETCVFPTSFAQRRLWFLDQLEPGSAVYNMPASFRTRGPYDVDSLVRS VNEIVRRHESLRTTVDVIDGEPVQVIAPSLRIEVPVVDLSEIDEPERAEARRLMAEESRRPF DLTRGPLLRAKLLRLGEADHVLILTMHHIVSDGWSMDVLFKELSTLYAAFHEGRPSPLPELPI QYADFAVWQRELLQGEVLESHLGYWREHLRGAPTLLELPMDRPRPPAQTFRGSQRAFRLPLSL QQAVQALSRQEGATPFMTLLTAFSVLLSRYARQSDLVVGTPIANRTRAELEGLIGFFVNMLAL RIDLGGDPSFRELLGRVREVTLGAYAHQDLPFERLVEELSPGRSPSHSPLFQVSFTLQNTPMD

ATNRADIASGGAPLVEMKAAKFDLĮLELSESPQGLLGTFEYNTDLFDAGTIERMAGHLEVLLS SAVAAPDRPIAELPLMGAEERSRVLVEWNSTAALYPEDHCMHELFEQQVERSPEATAVLLQQQ TLTYRELNMRANQLAHHLRSLGVGPEVRVGLYLERSIETVVAILGVLKAGGAYVPLDPTYPSE

15 RLGLMMADAAPSVLLTQASLLSKLPPHGDATLVQLDALHEALSRLPHHTPRSGVTAQNLAYVM
YTSGSTGRPKGVLVEHRGLCNLPTVQAKLYGIAPGDRLLQFAPLCFDTSFCEIALALLSGATL
VMGTADELLPGPPLVELLKKHAVTAMLLAPTVLAALPEQQSAALPLRVLTMAGEACPAELVKR
WKAPGRRLFNSYGPTETTIWASSAADLSDERIPPIGRPIANTQIYVLDEALEPVPIGVPGEIF
IGGVGVARGYHGRPDLTAERFVPDPFGQTKGARLYRTGDRARWLPDGNLEFLGRNDEQVKVRG

VRIELEEIRAALLKHPAVAQAVAVVREDTPGDKRLVAYVVGRGGARVTAAELRQSVSERLPAT MVPSSFVALDALPLTPNGKVDRRALPEPEQSAGGEDHVAPRNAVEEELARIWASVLRLERVGV HDNFFEIGGDSILSIQIVVRAQQAGLRLTPRQMFQHQTIAELSTVARAVEAVHVEQDPVTGPA PLTPVQRWWLEQEAAEPHHFNQSIFLEVRERLDESALEQAIAHLIDHHDALRLRLARDERGAH QVFAAPGGSTPFQRVDLGALPSAEQISAMEKAASEAQASLDLAAGPVVRAVLFDLGEVAPQRL

LVIAHHIAVDSVSWRILLDDLFGAYEQARRGEAVRLPPKTTSVKRWAELLTEHAGSEAVKAEL
GYWLDSSRRTVAPLPVDRRAGEDVWGSARHIVVSLTPEQTEQLLREVPQAYRTRIDDALLTAF
AQAIARWTGSPAVLLDLEGHGREELAGVDLTRTVGWFTAMYPILLRVDAADPGEALKSIKEQL
RAVPGRGLGYGLLRYLRSDTIAEVRALPQAELCFNYLGQLDQAIPEAAPFRPAREYQGSERSP
GAHRAHLIEVNASIANGRLYATWTYSERRHEPETIERVAASFVTALRALIAHCTLPEVGGNTP

30 SDFDKVRLRQETIDALDAIDAGPGPSARGSRIEDVYPLSPLQEGILFHTLYATDYTAYVEQFH

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		WTLEGDFDAEAFTRALQDVVARHAALRTSFAWERLDAPLQIVRTGAVLPVEHQDLRGLAAEEQ
10		TAHISRYVEAERQRRFDLRKAPLMRAGLLRLRKDAWCLVETIHHLILDGWSTQILLKEVFTLY
		EAHRGHRCHLALELEQPRPYGDYIGWLAKQDQVRTAAFWRRELEGFSAPTPLGVDRAVPHDDG
•	•	GPRFGWRRIALSGDDAARLAAFARQHQLTMSTLVQGAWALLLSRYSGDPDVLFGMTVSGRSAP
	5	IPGIERMTGLFINTIPVRVREPADASVLAWLKALQEHEAELLEHEHSPLVEVQAHSDVPRGTP
15		LFESLVVFENYPVQVIFEAPPVEGPTRAEEGLRMIDAQYISDPPYPLTVVAAFHGTLYLNIGY
		ERRRFDDQAVERMIGHVTTLLRGFVQRPETSVRDLPLLTAEEERTQLHAWNATAAPYPEGHCM
		${\tt HELFEQQVERSPEATAVLLQQQTLTYRELNIRANQLAHHLRSLGVGPEVRVGLCLERSIETVV}$
20		$\verb AILGVLKAGGVYVPLDPTYPSERLGLMMEDAAPSVLLTQTSLLSKLPPHGDATLVQLDALHEA $
20	10	LSRLPHHTPRSGVTAQNLAYVMYTSGSTGRPKGVLVEHRGLCNLPTVQAKLYAIAPSDRLLQF
•		APLCFDTSFCEIALALLSGATLVMGTADELLPGPPLVELLKKHAVTAMLLAPSVLAALPEQQS
		AALPLRVLAMAGEACPAELVKRWKAPGRRLFNSYGPTETTIWASSAADLSDERIPPIGRPIAN
25		${\tt TQIYVLDEALEPVPIGVPGEIFIGGVGVARGYHGRPDLTAERFVPDPFGQTKGARLYRTGDRA}$
		${\tt RWLPDGNLEFLGRNDEQVKVRGIRIELEEIRAALLKHPAVAQAVAVVREDAPGDKRLVAYVVG}$
	15	${\tt RGGARLTAAELRQSVSERLPATMVPSSFVALDALPLTPNGKVDRRALPEPERSAGGEDHVAPR}$
		NAIEEELTRIWADVLGAKRVGVHDNFFDLGGHSLLLVRVHDRLGQRFDRPPSMVDLFTYPTVA
30		SLARFLGERANGKOSPREAAADVTERGRRRLEARARRAKAIRGPT

SEQ ID No 28 (>ORF10)

MKHNIGWLLPAALATLAFVPACSPNHGEDAPSVTSAESGAAPSADCVALGAKLQAALDGAAAA

QKAPGAAAAVQSGDCVWRGATGVSDLVASTPTKPGDLFRIGSITKTFVSTLILMLRAEGRLSL

DDAVSKYVKGIPAGDQMTLRQILGHTSGLFDYTYSPALGQMIEVDPTRAFAPAELIALATAEA

PYFAPGAGFRYSNTNYIVAGLVAEAVSGGTLAGLLRTRILDPVGLAHTYLDGAEPPVQGLIRG

YGDYGAGLVDITDQLSPTEAWAAGALVSNVDDLNRFFALLISHELLSSDELQDMTTWTPTMWP

15 HEPGYGLGLIERDSALGSLNGHCGIIWGFQSASYGVPGRGDAITALINRSDGDAARLVDELAK

VVKER.

SEQ ID No 29 (>ORF11)

MSIDRAVLEQLDRVGGRLAEGKALKLLEDIAWPREVEERFFAAGEDRLPEVEYRVDRDGLARR
30 VAELRELLGAIDGDAPALGWLRDNVRAQIQAAELLEAAGTRAFSARSQELYGGARSRFFGGSL

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10		RNIDLAEHLTERLRVHGWDEASDPEEEPLDAGALRDMLAARVAGRAPRLDLEITVDPRVTAKV VAGMSRVRIRPEATFAAWEAEGLWHHEVETHALTAHNGAAQPRCAFLRSGGPRTTRTQEGLAI FAELYSRSLSIGRLTRLAERVRLVDMAEQGASFLDLYRHLRERGAERRDAYFDAQRVCRGGLV EGGAPFTKDACYLAGLLEVYAFLAAVLRGGLRDEVELLVCGRIALDDIAVLAELRAAGVLERP
15	5	RYLPGWLRAWQTLLPYFAFTSFMDGIDLGPVERHFQELLRVAADARPAGEGRRRRGRPREG
20	10	SEQ ID NO 30 (>ORF12) MSESVAQLEEHRAALTGHCYRMLGSVVDADDAVQETMVRAWRSLDKFDGRSSLRTWLYRIATN VCIDLRADRARRARPIEEGPVGTVDDALETRPRTHWLEPVPDAHALPADIDAAERAMLRQSIR LAFVAALQHLPPKQRAALLLTEVLGWSAAEVADSLNTSVAAINSALQRARATLASRDLGDARP SLPEPQSALLDRYVNAFERYDVDALTALLHQDATLSMPPFTLWLRGHESIRAWLVGPGAGCRG SRLIPTAASGSPAFAQYRPAPEGGHRAWALIVLDVAGDRIVSMTSFLDTETLFPRFGLPLDLP
25		A .
30	15	SEQ ID No 31 (>ORF13) VTIASIDHRDQDLMTGPQAKAPARAAAPDAAPSRRAVWAGRVLSGLATLFLTFDAAVKVLKLF PAEASTAELGFPAHLVPTLGYLQIACLVAYLIPRTAVLGAILWTGYLGGAIAIHVRVENPLFS HTLFPIYVAAFLWAGLWLRDRRVRALTASPSSQGR
35	20	SEQ ID No 32 (>ORF14) MTTKNPRKLFVNLSVRDLKRSMEFFSKLGFEFNPQFTDEKAACMVVSEEAYVMLLVESFFKTF MKKEICSTSTHTEGLFALSCSSRAEVDDMVKKAVAAGGSHAMDPQDHGFMYGWSFYDVDGHHW EVMWMDPKAIQP
45	25	SEQ ID No 33 (>ORF15) MTPSERLDATFAALADPTRRAILARLASGEASVTELAKPFAMSQPAISKHLKVLERAGLISRG RDAQRRPCRIEAKPLEDASGWLDNYRRFWEGSYERLDDLLEELKERESKGERSKR
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SEO	TD	No	34	(>ORF16)
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VAPASAPAAGGRDAAPFLDEAAQWLRGEQAPASRPAGEGPAGRLPGRVLVADDNADMREYALR LLVAEGWTVEAVADGRAALERARAHPPDLVLTDVMMPRLDGFGLLRALRADDRTRGVAVVMLS $A RAGE {\tt EARVDSLEAGADDFLVKPFSAKELLARVRIHVELARRREAEGQRQYLNDLFMQAPGP}$

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- IAILRGPEHVFEVVNPLYQRLVGGRSLVGEPIRAALPELEGQGIWELLDAVVRTGEPIVGKEL ${\tt PVRLDRRGDGTTEEVFFNFVYQPMRDRDGAVEGVFVFAFDVTDQVRARRRVEALVEALKLADQ}$ RKDEFLAMLAHELRNPMASISLSLTLLDDADGDGPASARYREIARRQMGHLVRLVDDLLDVSRITRGTVELRLEDVDLAAVVQSAAAAVRPAVEARRHDVSLSVGPGDFGMRADATRLEQVVTNLL ${\tt TNAAKYTPPGGSISVRLTREAAVGAPEAVLRVRDTGRGIPAAMLEKVFDLFTQVDQTIDRSTG}$
- GLGLGLTLVRRLLELHGGSVAAASAGPGQGSEFTVRLPLGPGAAPQPAPSAGPPPPREGPPPA 10 QRDEPPPPPAQRAEAPEAAADRRRVLVVEDAEDVRRVMRAYIEALGHEVTVAVDGLEGVKKLL $\verb|ELRPEVAFVDIGLPGIDGYEVARRARAAPGGEALYLVALSGYGGPDDQARSRRAGFDLHLTKP|\\$ VVGATLQDVLTAPRT
- 15 DNA sequence according to claim 7 selected from the fol-9. lowing
 - (a) open reading frames, and peptide sequences corresponding to said open reading frames:

pEPOcos6 ORF1 sequences:

(1) nucleotide sequence

Seq ID No 35 (>pEPOcos6_ORF1.seq)

 ${\tt GGATCACCTGCGGCGCGATCGCCGACCTCGTGCTGGTGTTCGGCTCGCTGGATGAGAAGCCGG}$ 25 CGGCGCTACTGATAGAGACGGCGACGCCCGGGCTGCGGGTGGAGCGGTTGCGGGAGATGCTCG GCTTTCGGGCGGCCCCCCGAGGCTGCCTTCGACGGTTGCGAGGTCCCCGAGGCTCAGC TCAGCGTCGCCTGGGCCTGGCCATGATCCGCGCTTGCCTGGAGACCTGCGCACAGCACA TCCTCACCCGCCGCACCTTCGGCCACCTGCTAGCCGATCACGGCATGATCCAAACCCTGATCA

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CCAACCTGGGGATTCACCACCAGGCGACGCTGCTCCACACGCTGCAGGCCTGCCGCGCCAGGG
ATCGCGGCGACGTGACCGCCTCCGAGGCCACCCTCGCCGCCAAATACCTCGCGTCGCGGACGG
CGGTCCACGAGACGACCAACGCGGTCCAGATCATGGGCGCGCTGGGCTGCGACGAGGAGGGCG
CGATCGCCCGCCACTTCCGCGACGCCAAGACGACCGAAATCATCGAAGGCAGCAACCAGATCA
TCGAGGCGCTGCTGGCCAAGAACATCGCCCGCGCCGGTCGCGACAACTATCGCCGCTTCCTCG
ATGCGGAAGTCGAGCCCGGTCGGGCCGACACCA

(2) peptide sequence

Seq ID No 36 (>pEPOcos6_ORF1.pep)

ITCGAIADLVLVFGSLDEKPAALLIETATPGLRVERLREMLGFRAAHLAKLSFDGCEVPEAQL
IGRPGFALMYLAPYALDFGRVSVAWACLGMIRACLETCAQHILTRRTFGHLLADHGMIQTLIT
NLGIHHQATLLHTLQACRARDRGDVTASEATLAAKYLASRTAVQETTNAVQIMGALGCDEEGA
IARHFRDAKTTEIIEGSNQIIEALLAKNIARAGRDNYRRFLDAEVEPGRAGGAP*

15 pEPOcos6_ORF2 sequences:

(1) nucleotide sequence

Seq ID No 37 (>pEPOcos6_ORF2.seq)

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 $\tt CTTCAGGTGGCGGGCCGGGCCCGAGATGGCGGACCAGATGAAGGGCCTGCGCTACGTCTTC$ ${\tt TGCAGCGGCGAGGCCCTGGCGCCCGGCCCACGTGTCAGCCTTTCAGGAGCACATCAACCGAGCG}$ 10 GGCAGCATCAGCTTGACCAACCTCTATGGACCCACCGAGGCGGCGGTCGACGTCAGCTACTTC GACTGCCCGCCCGGCGCGTCACTCGCGCGGGTGCCGATCGGACGAGCGATCACCGGCATCCAG $\tt CTGCTGGTCATGCGCGACGGCGTGCCTCAGCCGCCCCGGCGTCGAGGGTGAGCTCGCCATCGGC$ GGCGTTGGTTTGGCGCGGCGGCTACATCTCACGGCCAGACCTGACCGCCGACCGGTTCGTGCCG 15 GGCGAGCTGGTCTTCCTGGGGCGCATCGACCATCAGGTGAAAATTCGCGGTCTGCGCATCGAG CCCGGGGAAATCGAGGCCCAGATCAGCGCCCATCCCGATGTGGCCGACTGCGCGCTGATTATC 20 ${\tt GAGCAGGACTCGGAAACCCTGCCCLAGCTGACCGCCTACATTGTCGTGGCGCGACCGGGCTTG}$ 10 ACCCGGAAGGCGCTGCTACAGTTCCTGGGCGCGCGGCTGCCCGACTACATGCTCCCGAACCGC GGCCCGCTCGAGACCCTGCCTCTCCCTTTCTCC 25

15 (2) peptide sequence

GPLETLPLPFS

Seq ID No 38 (>pepocose_orf2.pep)

MTSAVPTRQTSLLDDFERVADVDPERIAVHASETSLRYGDMNARANRIAHGLRARGIGPNQIV
AVAMARTPELMIVLYGILKAGAAYMPIARDAPPLRRDHMLRESQAALMIADEEIAGLAARVLT
PADPFFAAMPDHNPEPRHDPTDLIYVIYTSGSTGQPKGVAMEHRAVWNRLTWMQAQYPIDTQD
VILQKTPIVFDVSVWELFWWPLAGASVALLPQSMEKFPWAISATVARCGVTVMHFVPSMLMAF
LQVVAGRPEMADQMKGLRYVFCSGEALAPAHVSAFQEHINRAGSISLTNLYGPTEAAVDVSYF
DCPPGASLARVPIGRAITGIQLLVMRDGVPQPPGVEGELAIGGVGLARGYISRFDLTADRFVP
HPGGDGQRLYRTGDLVRRDADGELVFLGRIDHQVKIRGLRIEPGEIEAQISAHPDVADCALII
EQDSETLPKLTAYIVVARPGLTRKALLQFLGARLPDYMLPNRFLTLTELPVTANGKRDWRALL

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pEPOcos6_ORF3 sequences:

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(1) nucleotide sequence

Seq ID No 39 (>pEPOcos6_ORF3.seq)

5 ATGTTACACCCGATTCCCACCGACCGTTTCGCCCTGAGCCGACCGCTCTTTCGCGGGTACCTC GCGCACGATCCGATCGTGCAGGCGTGCTGGCGGCGACCATCCAGGCTGGGTCCTGGTGGAC CGCGAGCCCGAGCCGCGCGCGCTGCTGTGGGCCTTTTCCGATCGGCTCTTCTGCGTGGGC GCCCGTAAGATCGGGCAGCCGTTTTTCCAGGTTCAGGGCGAGACGGTCGACACCTGGTCGGAC ${\tt CACCTGCATCAGGTGTCGCCGCACGCGACAGTCTCCTTCCGCCAGGCATTCCGCTTCGACCGC}$ 10 GACCTCTTCGAGCGGCTGCCAACCAAGCCGGAGCTGGCAGAGGCGCGGCTCGTGCCAATCGAC ${\tt GCGCGGCTGCTGGCCGAACAGGCTGATCTGCGCGAGCGGATACTGGCCTCCTGGTCCAGCGAA}$ GCTGCCTTCCATGCGCGGGTTTCGGCTTCTGCTACCGCGTAGGTGACCAGCTGCCGAGCGTG TGCCTGGCATCGCACGTAGGCGGCGGCGGCCGAGCTGAGCATCAACACCGAGCTCGAAGCG 15 CGCAATCGAGGTATGGCAACGCGGCTGTGCCGGCGTTTCATCGCCGAATCGCTGCAGCGCGGC $\tt CTGACGCCTTGCTGGGGCACCGAGACCTTTCGCCTGCCGTCAATCGCGCTGGCCCAGAAGCTC$ GGTTTCATCCCGACCTTCACCTTCCCCACCTACTGCTTCGCGACCGGCACCGAACAGCCGGAC GACAACTTCCTAGGCGAGCTGTACTACAGGGAATCGCGCATCGCCGGAAGTGGGACCGATGAG ${\tt CCGCAAGCGGTTCGGCTGGCGGGGGTTGGAGCCTGGCCGGGGGACACCGAGCGTGCCGCGAGC}$ TTCGCCGCACGCCCCTGGCCGAAGGGTGGGCCGGCCACTCGACTCTGGCCACCGATCCGGAT 20

(2) peptide sequence

Seq ID No 40 (>pEPOcos6_ORF3.pep)

25 MLHPIPTDRFALSRPLFRGYLAHDPIVQGVLAGDHPGWVLVDREPEPRTALLWAFSDRLFCVG
AADTLTPHALAELFHDRLIPQARKIGQPFFQVQGETVDTWSDHLHQVSPHATVSFRQAFRFDR
DLFERLPTKPELAEARLVPIDARLLAEQADLRERILASWSSEAAFHARGFGFCYRVGDQLPSV
CLASHVGGGAAELSINTELEARNEGMATRLCRRFIAESLQRGLTPCWGTETFRLPSIALAQKL
GFIPTFTFPTYCFATGTEQPDDNFLGELYYRESRIAGSGTDEPQAVRLARGWSLAGDTERAAS
30 FAARALAEGWAGHSTLATDPDFAELRASAAWPRLNVP

TTCGCCCGATTGCGCCCCAGCGCCGCCTCAATGTCCCT

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pEPOcos6_ORF4 sequences:

(1) nucleotide sequence

5 Seq ID No 41 (>pEPOcos6_ORF4.seq)

ATGATTTGTCACTCCCACCGCTTCATTTTCCTCCACGGTCCCAAGGTCGCCGGCACAAGCGTC

AAGGACGTCCTCGGCCAAGAGCTATTCCAGGAGGACCAGGTCACGTTCCAGATCGCTCCCAAT

CCCCACTACCCACCTGAATGGACTGCGCCTTACGAGGAGCACATTATTGCCGCTGAATTGAAG

AGCCAGTTGGCGCCGGAAATTTGGGACGATTACTTCAAGTTCGCCTTCGTGCGCCACCGCAC

10 GACTGGGCGGTCTCCAATTACTTCTTCTTCCTGCGCGACAGGCCATCCGGCCCACGAA

TTCCTGGAGCGGAAGGGCTTCGCCGGTACCATGGACATGTTTTTTCGGAGCGGCCGGGCCCAT

CCGCTGGTCGCCGGCATGCGCTTCAGCCAATGGGAGTTCTTGTGCGACAGCGAGGCCGGACG

CTGGTGGACTTCGTTGGCAAGTACGAGCGGCTCGAGCAGGACTTCGCCGCCGTGTTATCCGC

ATCGGGCTGACCCCGCCCGACTTGCCGTGCCTCAACCAGACTCGCCACCAATCCTTTACCAGT

TACTACGACGAGGCTTTGATGCGCCAAGTCAGCCGCGGTTTTCGAAATTTTTT

GATTATGCC

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(2) peptide sequence

Seq ID No 42 (>pEPOcos6_ORF4.pep)

20 MICHSHRFIFLHVPKVAGTSVKDVLGQELFQEDQVTFQIAPNPHYPPEWTAPYEEHIIAAELK SQLAPEIWDDYFKFAFVRHPLDWAVSNYFFFLRDRKGHPAHEFLERKGFAGTMDMFFGAAGRH PLVAGMRFSQWEFLCDSEGRTLVDFVGKYERLEQDFAAVCIRIGLTPPDLPCLNQTRHQSFTS YYDEALMRQVSRALARDFEIFDYA

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25 pEPOcos6_ORF5 sequences:

(1) nucleotide sequence

Seq ID No 43 (>pEPOcos6_ORF5.seq)

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GAGGGCCGCTCGACGTAGCGCGCTTCCGCCGCGCCTGGGAGCGCGTGGTGGCGGCTCACGAC 10 CTCTGCCGGACTGATACCCAACATCACGTGATGCTCCTCAGCAATCACCATATCCTGATGGAC GGTTGGAGTACGGGCCTGATTCTGCGGGACTTCCTCGCCTGCTACGGCGACTCCGAAAACTGG 15 CGGCCACGCACCCGAACGCACTTCAAGGCGTTCATCAAGTGGCACCAGAACCGGCCACGCCGG GGCGAGGAGCGATTTTGGCGCGACCTGTTGCGCGATGCGCCGACGGCGGCTTTCCCCGCCTG GGCGTCGAAGAAGGCACCCGCCACTCGCTTGACTTCGGCGCCCCGCAGCCGCGCTCTCGACGAC 20 10 CGCTTGACCCAAGGCTTGCCCGACATGGCTCGCCGACCTCGACGTCACCCTCGCCGCGATGCTC CATACCGCTTGGGGCCTTCTACTCCAGCGCTACCAGAACAGCTGCGAAGTGATATTCGGGACC ACCGTTTCCGGCCGCAACGTCGAGCTCGCCGGCCTCGACGAGGTGGTCGGCTTGTTCATCAAC ${\tt ACGATTCCGTTCTCGGCCGCCGCGGCCGACGACGCCCGTCGAGGCCTTCCGTGCGGTA}$ 25 CAGCGCAATCTGCTGGCGAGAAGCGAGTTCGAAGCCACCCCGCTGGTGGACATCAAGGGCTGG AGTGGTCTCGGTCCGGGCGCGGAACTGTTCGACACCATCCTGGTCATCGAGAACTATCCCTTG 15 30 ACCAATTACGGGCTGACCCTGACCATCGAGACCTTCAGCCGGTTGCACGTGACGCTAGCCCAT $\tt CGCCGTGACCTGCTGGGCGACGCGGCCGCTGAGCGAATGCTAGATCATTTCACCGGCCTGCTC$ ${\tt CAAGCCATGCTGCGCTTCCCTCACCAGCCGTTCGCGCGCCTCGAGATGAAAAGCGAACACGAG}$ 20 GCCCACCGCGTCCTGCACCAACTCAACCAAACGCGTCAGCCGTCCCCAATCGGCTTTC 35 ACGCGCTGGACCTACGGCCAGCTGCTGGAACGTGCCCTGCGTCTGGCGGGACGGCTGCAGGAA GCTTTGCTGGGCCCGCTGTTCGCCGGCGCGCCCTACCTGCCGCTCGATCCCACCCTGCCGGCC 40 25 GCGGGGCCCACGCCGATCCATCCGGACCCTGCCGGCGCCAGCCCCGTTGACGTCATTTTTGCC TGTCAGGACGGCGCGCGAGCCCGCCTACCTGATCTACACCTCGGGCTCCACCGGCCAGCCC 45 AAAGGCGTCTGGGTTAGCCACCGCAACCTGATCAACTTCCTGACGGGCATGAGCGCAATCCTG $\tt CCGGTCGCGGCCGACGACGTGTTCCTCTCGCTGACTACCGTGTCGTTCGACATTTTCGGGCTC$

GACCCGGCCGCGGCTGCCAAGGCCATCTCCTGCCATGGCGTCACGGTTTACCAGGCGACGCCA TCGCGACTCCAACTTCAACTGGAGCACCCCACATTTGTCCGCGCCATCGGCTCCCTGACGACC 10 CTGCTGGTAGGCGGCGAACCCCTCCCAGCCGAGCTGCTGCGGCGCGTACGCGAAGTGACCGAT GCGCGTATCTTCAACCTCTACGGTCCCACCGAAACCACCATCTGGTCCACAGCCGGGGAGGTC ${\tt ACCGCGGCGGACGTCCCGGATATCGGCCGCCCGATCGCAAATACCGGCGTTTTCCTTCTGGCG}$ CGAGACGGCTCGATCCAGCCGCCGGGCCTGGTGGGCGAGTTGTGCATCGCCGGCGAGGGCGTG 15 $\tt CGCCTGCCCTTTGCCGGCAAGCTCTACCACACCGGCGACCTGGCCCGCTGGACCGAAGACGGA$ 20 10 GAAGCGCTGAGCGCTTACCTGGCCGACCGACTGCCGAGCTACATGGTACCCGAACGGTGCATC CTCATGAAGGCCATGCCGCTAACCGGCAACGGCAAGATCGACCGGCGCGCCCTACCCAATCCC 25 TTCGCCTTGACCGAGTCGACCCGGCAGGCGGCGCGCGCACCTTGGCCCGCACCGCCGGCGAG ${\tt CATCGGGTTGCCGAGCTGTGGCAGGCCTTGTTGCGACGCGAGGCGATCGGCTTGGACGAACCC}$ 15 TTTTTCAGGCCGGGGGAACTCATTCGGCTTGATTCGGCTTCACGCCAAGCTGGAATCCGCC TTCGGGAAGTCGTTCCCGATCACCGATTTGTTCCAGCATACCAGTATTCGCAGCCAGGCAGAA 30 GCCGCCCAAGTTGCCTCCTCGGCAGCTAAATCCCCAGGGGAGCGCGGCGCGGCGCGCGACGTCG 20 35 GGCCGATTCCCCGCCGCACCCGACCTCGACGCCTTCCTTGAACTGCTCACGGAGGGTCGCTGC GGCATTCGCTTCTTCAGCCAAGCCGAGCTGCGCGACGAGGGTCTCGACGCGAATCGAATCGCG TGTCATAACTATGTCCCGGCCAAAGGTTTCCTCGACCGGGCCGACCACTTTGATGCCGACTTC ${\tt TTCGGCATCCGGCGCGCGCGAGAAATCACCGATCCGCAAATTCGGCTTCTGCTTGAGTGC}$ 40 25 TGCTGGAACGCGCTGGAGCATGCCGGCTACCCGGCCGGCGGCGAGATCGGGCTCTTCGCC GGCTCCTCGGCCAACTATCACTGGCTCGAATACGTGGGCATTTCCGAGGAGAGCAGCAATCGA ${\tt TTCGCCGTCATGATTCAAAACGAAAAGGACTACCTGGCCACGCGGATCGCCTACCAGCTCGAT}$ 45 TTGAAGGGCATTGCCGTCACCGTGCAAACGGCCTGCTCGTCGTCGCTGACCGCGGTCGAGCTG GCCTGCGATGCGTTACACGCCGGCCGCGTGACCATGGCTTTGGCTGGTGGCGTTGGTCTGACC 30

 $\tt CGGGCCTTCGACGCCCAGGCGGCACGGTCTGCGGCAACGGTCTGGGCATGGTGGTGCTG$ AAACAGCTCGACGCGGCGCTGGCCGACGGCGATGCCATCCACGCTGTGATTAAGGGCATCGCG 10 GCCAACAACGACGGCGGCCAAGATCGGCTACACGGCGCCCTCGCAGAACGGTCAGGCGCGG GTGATCCGCGCCCCATAGGCTCGCCCAAGTCGCGCGGAGACCATCGGCTATGTAGAAGCC AGCCCGCGTCGCGGCTTCTGCGCCTTGGGTTCGGTCAAGTCGAATGTGGGTCATTTGGATGCG 15 AGCCTCCACGTCGACACGCCCAACCCGCAGATCCCGTTCGCCGACGGTCCGTTCCAGGTCAAC 20 3.0 ACCGCGGCGCTGGTCCGCCACCTGGCCGCGCATCCGGACCTCGCACCAGATGACGTTGCCTTT ACCTTGCACGCGGGCCGCAAACCGATGACCCACCGTCGTTTCCTGGTCGCCGCCGACCTCGCG 25 15 TGCCAGGTCTGGATGTTCGCCGGTCTCGGCTCTCAATACCCCGGCATGTGTGGCGGCCTCTAT $\tt CGCACCGAGCCGGCCTTTCGCGAGCAAGTCGACCGCTGTTTCGACCTCCTCGCGCCGCGTTGC$ 30 GATTTGAAGCCCTCGCTCTTCCCCGAGCCCGATCAGGCCATCGACGCATCAGCCCTCGCGGCC ATCGACACCGCCCAGATCGCCGTCTTCGTCTGCGAATACGCGCTCGCACGGATGCTGGAAGGC GCCGGCGTCTTCTCCCTGCCCGACGCCTTGGCAATCGTCCGCGAGCGTGGCCGGATCCTGGCG 35 GCGGCCGAGCCGGGCGCGATGGTCAGCGTGCCCCTTCCGGCCGAGCGCGTCGCGTCGCTGCTG GAGCCGCCGCTTGCCTTGGCCATTGACAACGGCCCCTCATGCGTGGTGTCCGGGCCGGTCGAA CCGGTGCGCACCTTCACCGCTCGCATGAAGCGGGACCGGGTCTGGGTGACGCCGCTCCAGGCC GAGCGCCCGATGCATTCGCCGCTGATGGCCGAGGCCGGCGGCTCACTGCGCGCCCATGTTGGCC 40 25 45 GATCTGAGCTCCTTGGTGCGCCACCAGATGCCGGAAGGCGCCGACGAGCCGATCGCACTGATC ${\tt CGTCATCGCGAAGATCCGGTGCGCGACGAAGACCTCCTGCTCGATGGCTTGGGCCGCTGCTTC}$

5 . 108

 $\tt CTGCCCGGTTACCCGTTCCAGGGTCCACGCTGCATGCCCGGCCCGGACTGCCCGGCCTG$ 10 ${\tt GCGGGCGAGCTGGGCCGGCCTGCGCGCTTCCGGTTGCGCGACCACCCTCGTCGAAGGTGGG}$ CTGGCGTTCGCGCGCTTCGCGGGCGCTTCCGCGCGAATCCCCGCGAGGAACAAGATCTCGCA 15 CTGCCGTCGCCGGAGCGCGACTCGCCGCTGGCGCCTGGAGCACCTCACCGAGCTGGGCTTC CACCATCTGCTGGCCCTGGCCCCAACTGGAGGCGGTCGGCGCCCCGAGGTCCGCCTCGCC GTGGTGACAACCGGCCTGGCGGCGATTGGCGGCGAGTCCGAGCTGCGGCCCGAGGTCGGGCTG 20 10 GCCCCGGGACCTGAAGAAATCGCGCTGCGCGCACCAGCCGTTGGGAGTTGGGCTACGAGCCG GTCGAGGGGGGCACCGTGAGCACCATCTCCTCGCGACTGCGCGAGGGCGGCGTCTATCTGATC 25 15 GAGTTCGTACCGGTCGCAGCTGCGATCGCACAGATGGAGGAGTGTGGCGCCCGCGTGATTCCC 30 GTCGCGCTCGACGTCACCGACGCCGACCAAGTGAACGCGTTGTTCGCCACCATAGAAGCTACG GTCGGCAAGATTGAAGGCGTTTTCCACATGGCTGGCATCGTTGACGGCGGCATCATTCGAACG CGCACGCGCGCTGCCGACGCCGTGCTGGCGCCCCAAAACGGTCGGAACCTGGATTCTCGAT $\tt CGGGCTCTCCGCGGCGCCGGTGGCCGCTTCCTGGTGCTGTACTCCTCGATCAACGCGGTCGTC$ 20 35 GCGCCCTTCGGCCAGGTTGCCTACGCCGCCCAACGCCTTCCTCGACGCCTTCGCCAGCGCC ${\tt CACGAACACGACGACGTCTTTTCCGCGTCAGCATCGGTTGGGACACCTGGCGCGAGGCCGGC}$ ATGGCCGTCGATGCCGCCCGCGCCGCGCGACCAGGCCCCGCTCGAAGGGCTTAGCGACGAG CAGGGCTTGCGCCTGCTCGAAAGCGCCTTGGTCGGTTGCGAACCGCGACTCCTCGTCTCCATC 40 25 CCCCGCGCCAACGAGGCGGGTGCAGCTGATTCCGGCGAGGGGGGCGCCACGCAAGACGCGTCG CCGGCCCGTCCCGATCTGGTCGTCGCCCGCCGGCCGGCAACGAGCTGGAG 45 ${\tt TTCAACGATTTGGGCGCCACCTCGCTCGACCTCATCCAGATCGCCCAACGCCTCGGTCGCGAGGCCTCATCCAGATCGCCCAACGCCTCGGTCGCGAGGCCTCATCCAGATCGCCCAACGCCTCGGTCGCGAGGCCTCATCCAGATCGCCCAACGCCTCGGTCGCGAGGCCTCATCCAGATCGCCCAACGCCTCGGTCGCGAGGCCTCATCCAGATCGCCCAACGCCTCGGTCGCGAGGCCTCATCCAGATCGCCCAACGCCTCGGTCGCGAGGCCTCATCCAGATCGCCCAACGCCTCGGTCGCGAGGCCTCATCCAGATCGCCCAACGCCTCGGTCGCGAGGCCTCATCCAGATCGCCCAACGCCTCGGTCGCGAGGCCTCATCCAGATCGCCCAACGCCTCGGTCGCGAGGCCTCGGTCGCGAGGCCTCGGTCGCGAGGCCTCAGGCCAGAGCCTCAGGCCAGGCCTCAGGCCTCAGGCCTCAGGCCTCAGGCCTCAGGCCTCAGGCCTCAGGCCTCAGGCCTCAGGCCTCAGGCCTCAGGCCCTCAGGCCCTCAGGCCCCCAGGCCCCAGGCCCCCCAGGCCCCCAGA$ 30

TTCCTCGGCGCGCGCTCCAATCCGCGCGGTCCGGCGTCCCGACGGGCGCTGCCGCACCGGGC GCCGCCACGCCGGGGGTTGCCACCCCGCCGCGGCCACAACCGTCGCGCCAGCACCTGGAAAAA CGCCGTCAATTGAGGAAAAAAGGGGGGCCTTCCCATCATGAG

5 (2) peptide sequence

Seq ID No 44 (>pEPOcos6_ORF5.pep) MKVDKRNVDDILGLTPTQTGILYHYLLDPQADAYFEQLTLHLEGPLDVARFRRAWERVVAAHD QLRAVFRWQGIEHPVQIILKQHVPDLELAEVPRDADPAAFLAQWVAADRARKFDFETVPFRIG LCRIDTQHHVMLLSNHHILMDGWSTGLILRDFLACYGDSENWRPRTRTHFKAFIKWHQNRPRR ${\tt GEERFWRDLLRDAPDGGFPRLGVEEGTRHSLDFGARSRALDDRLTQGLRDMARDLDVTLAAML}$ HTAWGLLLQRYQNSCEVIFGTTVSGRNVELAGLDEVVGLFINTIPFRFSAAAATTPVEAFRAV QRNLLARSEFEATPLVDIKGWSGLGPGAELFDTILVIENYPLDRAIFESDSSLRLTDHQIFER TNYGLTLTIETFSRLHVTLAHRRDLLGDAAAERMLDHFTGLLQAMLRFPHQPFARLEMKSEHE AHRVLHQLNQTRQPLPSQSAFHQLFFEQAQADGARPALWCGATRWTYGQLLERALRLAGRLQE ${\tt AGFARGDVAAVSLGPVPDLIPGLLGPLFAGGAYLPLDPTLPAQRSRFILDDAGCRFLISDAPL}$ AGPTPIHPDPAGASPVDVIFACQDGAAQPAYLIYTSGSTGQPKGVWVSHRNLINFLTGMSAIL PVAADDVFLSLTTVSFDIFGLETWFPLSRGCTIVLGTRAEQLDPAAAAKAISCHGVTVYQATP SRLQLQLEHPTFVRAIGSLTTLLVGGEPLPAELLRRVREVTDARIFNLYGPTETTIWSTAGEV TAADVPDIGRPIANTGVFLLARDGSIQPPGLVGELCIAGEGVALGYHRRPDLNRERFREIPPG RLPFAGKLYHTGDLARWTEDGRLLCLGRLDDQLKVRGHRVEPGEIEAVMARHPAVTQAVVVTR PRNGEPVLVGFWTAEGEPMPEEALSAYLADRLPSYMVPERCILMKAMPLTGNGKIDRRALPNP FALTESTRQAAPRTLARTAGEHRVAELWQALLRREAIGLDEPFFQAGGNSFGLIRLHAKLESA FGKSFPITDLFQHTSIRSQAEMLSGSSVEAPLAGAVPQPPAAAAQVASSAAKSPGERGAAATS SGLTAQPPQPHFRPIAVIGLAGRFPAAPDLDAFLELLTEGRCGIRFFSQAELRDEGLDANRIA $\verb|CHNYVPAKGFLDRADHFDADFFGIPPRDAEITDPQIRLLLECCWNALEHAGYPPGGGEIGLFA| \\$ GSSANYHWLEYVGISEESSNRFAVMIQNEKDYLATRIAYQLDLKGIAVTVQTACSSSLTAVEL ACDALHAGRVTMALAGGVGLTYPLRAGYLHEDGMIFSPDGRCRAFDAQAAGTVCGNGLGMVVL KQLDAALADGDAIHAVIKGIAANNDGAAKIGYTAPSQNGQARVIRAAHRLAQVAPETIGYVEA

HGSGTPLGDPIEVAGLTEAFDSPRRGFCALGSVKSNVGHLDAAAGIAGFIKAVLSLSHRTLFA SLHVDTPNPQIPFADGPFQVNTETRPWPAADHPRRAGVSSFGIGGTNVHAVLEEAPQLAEHAG

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RRREROLFLVSARTAADLERRTAALVRHLAAHPDLAPDDVAFTLHAGRKPMTHRRFLVAADLA EAAARLAEPDPVKSAAARADRCQVWMFAGLGSQYPGMCGGLYRTEPAFREQVDRCFDLLAPRC DLKPSLFPEPDQAIDASALAAIDTAQIAVFVCEYALARMLEGWGLRPDRLIGYSFGEYVAACL AGVFSLPDALAIVRERGRILAAAEPGAMVSVPLPAERVASLLEPPLALAIDNGPSCVVSGPVE ${\tt PVRTFTARMKRDRVWVTPLQAERPMHSPLMAEAGGSLRAMLAGFRLNAPRIPILSNVTGTYLT}$ DEQARDPDYWARHLCGNVRFADGVRTLLAERDPVFLEFGPGRDLSSLVRHQMPEGADEPIALI $\verb|RHREDPVRDEDLLLDGLGRCFLRGATLHGQALYAGRGCRRVPLPGYPFQGPRCMPARAGLPGL|$ ARPTVGATTISYRPAWKRAPRLAAVESLAPQSWLVFSDGSELAGELVAGLRASGCATTLVEGG LAFARFAGGFRANPREEQDLAQLFATLSAEAMLPTHILHLLSLPSPERDSPLARLEHLTELGF $\tt HHLLALARQLEAVGAPEVRLAVVTTGLAAIGGESELRPEVGLLRGPVRVIPFEFPNLRLRLID$ 10 LDSADPIWRSGCEPLLREMGAAPGPEEIALRGTSRWELGYEPVEGGTVSTISSRLREGGVYLI TGGLGGLGLALARHLARKYRATLILAGRRGAPARELWHQAPAEFVPVAAAIAQMEECGARVIP VALDVTDADQVNALFATIEATVGKIEGVFHMAGIVDGGIIRTRTRAASDAVLAPKTVGTWILD RALRGAGGRFLVLYSSINAVVAPFGQVAYAAANAFLDAFASAHEHDERLFRVSIGWDTWREAG 15 MAVDAARARGDQAPLEGLSDEQGLRLLESALVGCEPRLLVSISELRARLAEHHRNGGIPRLLG PRANEAGAADSGEEGATQDASPARRARPDLVVAFAPAGNELERRIVAIIGAYLRLGQVGVDDN FNDLGATSLDLIQIAQRLGRELGRDVPVVSLYQHRTVRGLSRFLGGALQSARSGVPTGAAAPG AATPGVATPPRPQPSRQHLEKRRQLRKKGGPSHHE

20 pEPOcos6_ORF6 sequences:

(1) nucleotide sequence

Seq ID No 45 (>pEPOcos6_ORF6.seq)

ATGAGTGAAGTATCCATTCGCCCCGGCTTGGACATCGCGGTCATCGGCATGGCCTGCCGCTTT

25 CCCGGTGCCCGCAACCTCGCCGAGTATTGGGCCAACCTGATCGAAGGCCTCGAAACGCTCAGC
TTCTTCAGCGAAGAGGAGCTGCGTGAGGCCGGCTGCGATCCGGTCCAACTGGCCCAGCACAAC
TACGTGCGCACCAAGGGCCTGCTCCCTGACGCAGACCGTTTCGACGCCGATTTTTTTGGTTAT
TCCCCGCGCGAAGCCCAGGTGATGGACCCCCAGATCCGCGTCTTCCACGAGGTCTGTTGGCAG
GCGCTGGAGCACGCGGGCTACAACCCGCATCGCCACACCGGCACGATCGGCCTGTTCGCCGGC
30 GCCGCGCCCAACGTTTTTTGGGAGTTTCTCTCCTATCGGTCCGATGCCGCCAATTTAGGCAAC

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 ${\tt TTCACGCTGGGCCTGCACAACAACAACGACTACCTGAGCTCGCGCATCGCCTACAACTTCAAC}$ CTGACAGGGCCCAGCTACACCCTGTTCACCGCCTGGTCGACCTCGATGGTCGCCATCCACCAG GCCGTCCAGGCGCTCCAACGGCGAATGCGACCTGTGCATGGCCGGCTCGGTCTCCATTACG CTGCCACTGGTTGCCGGCTACACCTACACGCCGGGCATGATCGTCTCGCCCGACGGCCATTGC AAGCGGGCCGAGGATGCGTTGGCCGACGGCGACCACATATTTGCGCTCATCAAGGGCTCGGCG CTCAACAACGATGGCAGTCGCAAGACCGGCTACACCGCGCCCCAGCGTGCAGGGGCAGGTGGAG GTGATCCGCGCGGCGATGAACCTGGCGGAGGTCGAGCCGGAGGCGATCAGCTACGTGGAAACC CACGGGACGGCCACCGCTGGGCGATCCGCTGGAGTTCGAGGCGCTAAAGGAGGCCTTCGGA GGTGGCTGCAAGGCCTTCTGTGGATTGGGTTCGGTCAAGCCGAACATCGGCCATCTGGACGTG 10 ACGCTCCACTTCCAACTGCCCAACCCGAAGATGGATGTGGTCGATAGCCCCTTCTACATCGTG GCTGAGCGCGAACCCTGGCGCGAAGATCTGCTGCCGCGTCGGGCCGGTGTCAGCGCGTTCGGT CTGGGTGGCACCAACGTCCACATGATTTTGGAGGAGTTTCAGCGCGAACCGGCGGCGAACAGC GCGCGCACGCGCCACCTGACGGTGCTGACGGCGCGCTCGCCGCAAGCCCTGGCGCAGCTGGCG 15 GCCAACCTCGCCGAACACCTGCGCGAACACCCCGAGTTGGCGCTGGCCGATGTGGCCCATACG $\tt CTGCTGCACGGCCGCAAGCCACATCCATTCGCGCGCATCCTGGTGGCGACCGATACGACGGCG$ GCGATCGACGCCTTGATGAACGACCGCGATCCGCGAACGCGTTTCTTCGAAGCGACCGGGCGC ${\tt GGCGAGTCGGTGATCCTGTGTTTTGACGAAACGCCGCCGGAGCCGCGAAGCGCCCGCTACCTC}$ 20 TGGGATCACGAGCCGCTTTATCGCGCGGCGGCGACGTCGTGCTTGGCTGGTGAGGTCGCCGAC CCGGATCTGGAAGGCTGCTTTACTGCCCTGATCGCCGAGCAGGCGGCGGCAGCCGCCTTTTGC GTGGGCCAGGGCGAGTGGGTAGCAGCGGCGCTCGCGGAGGTGTTCCCGCCATCGGCCTGCTTG 25 AATTTCTCTGGAAACTGGATCGTTGGGCGTGAGTTGGCCGGACCCGGATTACCCCAGAAAGCAG AAGGGTAAGCGCTGCATGAAGCGCCGTCGGTCCCAACCTCGGTCAGCTGGTGCAGGATGGGGG CGATGGAACCGGCTCGGTCAGCTCGTCGCGCGCTCTTTCCGCGGGAAGCGGAGGCGGGACG GTGATCGGCCCGAGGGCGAGGTTCATCTCGTCGTCGACGAGCCGGGCGCGGGGGGCGCGCCCAG TACCTGGGGGCGAGCTCGAGG

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(2) peptide sequence

Seq ID No 46 (>pEPOcos6_ORF6.pep)

MACRFPGARNLAEYWANLIEGLETLSFFSEEELREAGCDPVQLAQHNYVRTKGLLPDADRFDA

DFFGYSPREAQVMDPQIRVFHEVCWQALEHAGYNPHRHTGTIGLFAGAAPNVFWEFLSYRSDA

ANLGNFTLGLHNNKDYLSSRIAYNFNLTGPSYTLFTACSTSMVAIHQAVQALLNGECDLCMAG SVSITLPLVAGYTYTPGMIVSPDGHCRTFDAGANGTVYGDGAGVVVLKRAEDALADGDHIFAL IKGSALNNDGSRKTGYTAPSVQGQVEVIRAAMNLAEVEPEAISYVETHGTGTTVGDPLEFEAL KEAFGGGCKAFCGLGSVKPNIGHLDVTSGIASFIKLVLALEHRILPPTLHFQLPNPKMDVVDS PFYIVAEREPWREDLLPRRAGVSAFGLGGTNVHMILEEFQREPAANSARTRHLTVLTARSPQA

LAQLAANLAEHLREHPELALADVAHTLLHGRKPHPFARILVATDTTAAIDALMNDRDPRTRFF
EATGRGESVILCFDETPPEPRSARYLWDHEPLYRAAATSCLAGEVADPDLEGCFTALIAEQGA
AAAFCHQYALAGWLLAMGLTPSALIGVGQGEWVAAALAEVFPPSACLRWIRFGERLPQPRDQR
IPFLSNFSGNWIVGRELADPDYPRKQKGKRCMKRRRSQPRSAGAGWGRWNRLGQLVARCSSAG

SGGGTVIGPRARFISSSTSRARVRAQYLGASSR

pEPOcos6_ORF7 sequences:

(1) nucleotide sequence

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Seq ID No 47 (>pEPOcos6_ORF7.seq)

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AGCGCCTCTTGGTGGTGTGCCGCGGAAGAGGGGCGTCATAGATGGCGTGAGCGTCAGCTTGAAT ATACCGAGAGAGCCGCGGAACATCTCGCAGACCGCGGCGCTGGTATGCTTGGGCTGGTACTC CAAGAAGACGTGATCCTTGTCCGCGAGGACGACGAAGAAGTGTCCCTTGCGGCACGGCCCGGG ACCGACGTCTTCGGCGTAGCGGCACATCGTGCCGCGATCGAGCGCGCCCCTGAAGCTCCAG CTGCTGCTCCAGTCGATAGAACGGGACGCCGAGCAGGTACTTGCTGGTGAGGATGTGCGCAAT CATCGACGCGCGAGGAACGACCGCCGGAACAACTCCTTCGGAAGCGGCGTCGTGATGAAGAC 10 GGAGGAAGCGCTCGCCGGCCGCCGCTGCCGTGTCCTCCGGGCTGACGCTCGCAGCGGGCGT CGGCGTCGGGGCTTCTCTCGCGACGACCTGGAGCGGGGCCGCTTCCTCCTCGCCCGAACTGCT GCCGCGCTCGTAGCCGAGTCGCGAGGTCTCCTCGACCCCGATGCGCGTCGCCGTCGCATCGAG $\tt CTTGCCGCCGGACCTTCGGCCCCTTGGGGTCGTCGTCGCCGCTCGTCGCCTGTATT$ 15 ${\tt GCGCTCGGCGCGTCGAGTGCCTTCGCGAGGCGCTCGAGGCACCTCGAGGAACATCGAGTCGAACGC}$ CAGCTGCTCCGCGCTCACCTCGGCGCGCCTCCGCCTTGGCCACGAACAGTCGACGTCGCAGAAG 20 CGAGAGCGTCGGCTTGGCGGCGCGTCGTGCACGACGCCGCTCTACGTAAGCCGCGCGTACTT GCGCCCTCGGTCGGGGGGTCGGGAAGTGCGAACGCTCCGCGATCAAGGCGTTTTGAAAACAGG CAGATTCCACTGCCATCGAAGAAGAGAATCTTGATCGTGGTCCGCCGCTTGCCGACGAACGCG 25 AACAGCGCTCCGCAGCGAGCCTCGTACCCCACACGCTCACGGATGAGACCCGAAAGCCGCTCG AAGCCG

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WO 00/22139 PCT/US99/23535

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(2) peptide sequence

Seq ID No 48 (>pEPOcos6_ORF7.pep)

MEPARSARRALLFRGKRRRDGDRPEGEVHLVVDEPGAGARPVPGGELEVAVPRPVGHRANDVG

QVGLRVEPVQLAARHEREEVGRGGGVVVAAEEEPGLSRNRNGSQRSLAGVVLQAQPTVVEEAP

QRLLLVEGVAERGGDQAALAGTSVLGPGPGKERVDQRADDDIATHLALRGRQVRQRAIGGKEG

VDAPQPLDTELVLADRRLPEVGTAMRPASDFGRGRTALLVGSSASWWCAAEEGVIDGVSVSLN

IPREAAEHLADRGAGMLGLVLEEDVILVREDDEEVSLAARPGLLVLALLDGPRLDGDPGGVRG

QAEGGLEGLFARGLDDGAQGRTDVFGVAAHRAAIERRALKLQLLLQSIERDAEQVLAGEDVRN

HRRREERPPEQLLRKRRRDEDRAGLALRRRRRRVERGRVERCGGSARLAGRCRVLRADARSGR

RRRGFSRDDLERGRFLLARTARIRDGPLGLVHDACEHDAAHSAALVAESRGLLDPDARRRRIE

RRRGFSRDDLERGRFLLARTARIRDGPLGLVHDACEHDAAHSAALVAESRGLLDPDARRRRIE LGAGELDADDGQVGLGQVATALAAGPSFRPLGVVVLPLVACIALGGVECLREALDLEEHRVER QLLRAHLGALRLGHEQSTSQKLQLLERTGVGAPKLRERIARSHELALCRGELRFELRDALLLG RERRLGGGVVHDAALRKPRVLVERIRAAQWTRRGARLRGLDVGAISMPSSSVSSVASSTSTCV APSVGGSGSANAPRSRRFENRQIPLPSKKRILIVVRRLPTNANSAPQRASYPTRSRMRPESRS

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pEPOcos6_ORF7.1 sequences:

(1) nucleotide sequence

Seq ID No 49 (>pEPOcos6_ORF7.1.seq)

ATGTTCCTCGAGGTCCAGCGCCTCGCGAAGGCACTCGACGCCGCGAGCGCAATACAGGCGAC

GAGCGGCAGCACGACGACCCCAAGGGGCCGAAACGAAGGTCCGGCGGCAAGGGCCGTCGCGAC

CTGTCCGAGTCCGACCTGCCCGTCGTCCGCATCGAGCTCCTGCCCCGAGCTCGATGCCACG

GCGACGCGCATCGGGGTCGAGGAGACCTCGCGACTCGGCTACGAGCGCGGCGGAATGCGCCGC

ATCGTGCTCGCACGCGTCGTGTACAAGGCCGAGCGGTCACGGATGCGAGCAGTTCGGGC

GAGGAGGAAGCGGCCCCGGTCCAGGTCGTCGCGAGAGAAGCCCCGACGCCGACGCCGCTGCG

AGCGTCAGCCCGGAGGACACGGCAGCGGCGGAGCGCTTCCTCCACAGCGCTCGAC

GCGCCCTCGCTCGACGGCCGCCGCCGCCGCCGAGGCCGAGCCCGATGCACGTCTTCATCACG

ACGCCGCTTCCGAAGGAGTTGTTCCGGCGGTCGTTCCTCGCGCCGTCGATGATTGCGCACATC

CTCACCAGCAAGTACCTGCTCGGCGTCCCGTTCTATCGACTGGAGCAGCAGCTTCGA

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 ${\tt GGCGCGTCGCTCGGTCGGGCACGATGTGCCGCTACGCCGAAGACGTCGGTGCGACCCTGGGC}$ GCCATCGTCGAGGCCGCGCAAAGAGGCCTTCGAGACCGCCTTCTGCCTGTCCACGGACGCC ACCGGGGTCTCCGTCCAGCCTGGGCCCATCCAGGAGCGCAAGGACAAGAAGCCCGGGCCGTGC $\tt CGCAAGGGACACTTCTTCGTCGTCGTCGTCGGGACAAGGATCACGTCTTCTTCGAGTACCAGCCC$ ${\tt AAGCATACCAGCGCCGGGTCTGCGAGATGTTCCGCGGGCTTCTCTCGGTATATTCAAGCTGAC}$ GCTCACGCCATCTATGACGCCCTCTTCCGCGGCACACCACCAAGAGGCGCTGCTGCCGACGAG AAGCGCGGTCCGCCCCCGACCGAAGTCGGATGCTGGTCGCATTGCCGTACCAACTTCTGGGAG GCGGCGGTCTGCAAGCACGAGCTCGGTGTCGAGGGGCTGCGGCGCATCAACGCCCTCTTTGCC GCCGATCGCGCGCTGGCGGACCTGCCGCCCGCGCAGGCGCAAGGTGCGTCGCGATGTCGTCGTC $\tt CGCCCTCTGGTCGACGCGTTCTTTGCCTGGGCCAGGGCCGAGCACGCTCGTCCCCGCGAGCGC$ ${\tt GGCCTGGTCTCCACCGCGCTCGGCTACGCCCTCAACCAAGAGCAGCCGTTGCGGCGCTTCCTC}$ GCGAGAAAGTCCTGGCTCTTCTTCGGCAGCGACGACCACGCCTCCGCCGCGGCCAACCTCTTC ${\tt TCGCTCGTGGCGAGCTGCAAGCTGCACGGGCTCGACCCGGAGGCCTACCTGGCCGACGTCATT}$ ACCCGCGCCCGGCTCGTCGACGACGAGATGAACCTCGCCCTCGGGCCGATCACCGTCCCGCCT CCGCTTCCCGCGGAAGAGCAGCGCGCGCGACGAGC

(2) peptide sequence

Seq ID No 50 (>pepocos6_ORF7.1.pep)

MFLEVQRLAKALDAAERNTGDERQHDDPKGPKRRSGGKGRRDLSESDLPVVRIELSCPELDAT

ATRIGVEETSRLGYERGGMRRIVLARVVYKAERSVTDASSSGEEEAAPLQVVAREAPTPTPAA

SVSPEDTAAAGEPSASSTALDAPSLDAPPPAPKGETCTVFITTPLPKELFRRSFLAPSMIAHI

LTSKYLLGVPFYRLEQQLELQGASLDRGTMCRYAEDVGATLGAIVEAARKEAFETAFCLSTDA

TGVSVQPGPIQERKDKKPGPCRKGHFFVVLADKDHVFFEYQPKHTSAAVCEMFRGFSRYIQAD

AHAIYDALFRGTPPRGAAADEKRGPPPTEVGCWSHCRTNFWEAAVCKHELGVEGLRRINALFA

ADRALADLPPAQRKVRDVVVRPLVDAFFAWARAEHARPRERGLVSTALGYALNQEQPLRRFL

DDGRLRLENNASERALRSIAVARKSWLFFGSDDHASAAANLFSLVASCKLHGLDPEAYLADVI

RAMPYWPRDRYLELAPRYWARTRARLVDDEMNLALGPITVPPPLPAEEORATS

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PCT/US99/23535

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pEPOcos6	ORF7.2	sequences:
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10 (1) nucleotide sequence

Seq ID No 51 (>pEPOcos6_ORF7.2.seq)

- 20 10 ACGTCCAAACCGCGAAGGCGCGCACCGCGCCGCGCCCAC
 - (2) peptide sequence
- Seq ID No 52 (>pEPOcos6_ORF7.2.pep)

MIPAGVQVFVALEPVDMRYGFERLSGLIRERVGYEARCGALFAFVGKRRTTIKILFFDGSGIC

- 15 LFSKRLDRGAFALPDPPTEGATHVEVDDATLETLLDGIEIAPTSKPRRRAPRRVH
- - (1) nucleotide sequence
- - 25 GGGTTCGACCCCGCGCTGCTGGCGGAGGTGGTCCGTGCCCTCGGCGGAGCGGGGCGA
 - (2) peptide sequence
- 45 Seq ID No 54 (>pEPOcos6_ORF7.3.pep)

 ${\tt MTRTKATEVMWSERVRAWRESGETAEEFARSRGFAASTLHGWSSRLSRAEPPRFLRLVPKAPA}$

30 VTSSAAELVVEVGGARVRVAAGFDPALLAEVVRALGGAGR

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pEPOcos6_ORF8 sequences:

(1) nucleotide sequence

5 Seq ID No 55 (>pEPOcos6_ORF8.seg) ACTGGACAGCGCAGCCGGGGTGAGACGGCGCTTCGCGCAGCGCTTACGCAGAAGGCGCGCCGC GCGCCATTGTCGGATGCGGTGCGCGACTTCGCCGCCGATCGGCTGTTGCTGGAACTGGGACAA GCCTACCAAGCGTTGGCCCAGCTCTGGATCTGCGGCGCCCTGGCCGAACCGCCGCGACTGTAT CCCGACGAACACCGCCGGCGCGCGCGCCGCCGAGCTACCCCTTCGAGGGAAAGCGGTTCTGG 10 $\tt CTCGGCGCCTGGCTGAGCGAGACCTTGCGCGACAAGGGCGCGCGGGTCGCGACAGTCGTTCGA$ 15 ${\tt GGCACCGAGTTCCGACGCCTTGGCGTCACAGCGCTTCCAGCTTCGTCCCGATCGACGGGACGAT}$ TACCGGACCCTGCTGCACGAGTTGAAGGCGCAGGGCATCGCGCCGGTCCACCTGTGCCACCTA ${\tt TGGAGCGTGACCGCACCGGATGCCGAGCAGTTGCTCGACGTCAGCTTTCACAGCCTGGTC}$ CATTTGGCGGCCGCTTTGGGTTCGGTTGGCTACTTCCACGCCATG

117

20 (2) peptide sequence

HLAAALGSVGYFHAM

Seq ID No 56 (>pEPOcos6_ORF8.pep)

TGQRSRGETALRAALTQKARRAPLSDAVRDFAADRLLLELGQPLDVTAEASQRLQLARGDLFG
AYQALAQLWICGALAEPPRLYPDEHRRRVPLPSYPFEGKRFWIEGSPFETAPAAGASPQPADS
GDILKGDPADWYYRPRFEAAPLLPSPFESEPGDWLVFEDELGLGAWLSETLRDKGARVATVVR

25 GTEFRRLASQRFQLRPDRRDDYRTLLHELKAQGIAPVHLCHLWSVTAAPDAEQLLDVSFHSLV

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pEPOcos6_ORF9 sequences:

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(1) nucleotide sequence

Seq ID No 57 (>pEPOcos6_ORF9.seq)

ATGAAGTTGAACGTGGTCGCCAACCGGCTATTCGACCCCGAGTCGCCCCGAGCGCACCGAGCCC GCCAAGAGTC'IGTTGCTCGCGGTGACCAAAGTCCTGCCGCAAGAGGTGCCCAACGTTCGAACC TTGTTGGTTGAATGCGGCGCCCCGTCCAGGAAACGGTGGTGACCTACCATGGCGCAGCCCGA TGGCTGCGCCGCTTCGATCGCGTTGCGGTGAATGGTCTCGGCCCGTTCCACCCCGATCAACCT 10 GATGTCGCCGACGAAGCGGCCATGGCGCAGGCGATCGAGGCCTCACTGGCGCGATTCGACGCT 15 AGTATGACGCGGGCCATGTGCGAGGAGCAGCTCCGCCCCAAGATGTTGGGCCTCGACGTCGTC ${\tt GACCGCCTCCTGCGCGATCGCCCGGTTGGACTTCCGCATTGCCATCTCGTCGCCCCGATT}$ 20 ${\tt CCGGCTACCTACGACGAGCGGGTGGGCCGTTCGCTCAAGCAGCTCGAGCTCACCAACGAGGAG}$ ATTTCCACCGGCGACCTCCAGGCCCGCCTCGACAAATGGATTCACATCAAATCCCTGCATCGC CGCGCCGCCTTCGAGGCCGCCTTCGCTGACGCCTGGTGCGACTTCTTCGGGGTTGAAGAGGTC CGCTTCAGCAAGGCCATCGAACAGCATGTACCGCTCGAGGCCCTGCTCGAACACTCCACCCTG CACGACCTCGCCGCCCACCTCGCGGGCGACGCGAACACCGACGCCAGCGAAGCGCGCATT

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CCGCTCGCGCCCGACCTGGACACCTATTGGCGCAACCTGGTCGGAGGCATCGACGCGGTCAGC
TTCTTCAGCGCCGAGGAGTTGCGTGCTGGCGTCACCGCGGGCCGAGATCCACCACCACCACC

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TACGTGCCGGCCAAGGGGCGCTGCGCCGACCAGGACTTGTTCGATGCGGCCTTCTTCGAATAC ACTGCCAGCGACGCCGAGCTGATGGACCCGCAAAATCGCGTGTTACACGAGGTCGTGTGGCAC . 10 ${\tt GCGCTGGAAGACGCCTGTTTCGACTTCAACGGCGATCACGGCCAGGTCGGCCTGTTCGCGGGCCAGGTCAGGTCGGCCTGTTCGCGGGCCAGGTCAGGGCCAGGTCGGCCTGTTCGCGGGCCAGGTCAGGTCGGCCTGTTCGCGGGCCAGGTCAGGTCGGCCTGTTCGCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCAGGTCAGGTCGGCCTGTTCGGCGGGCCAGGTCAGGTCGGCCAGGTCAGGTCGGCCAGGTCAGGTCGGCCAGGTCAGGTCGGCCAGGTCAGGTCGGCCAGGTCAGGTCGGCCAGGTCAGGTCGGCCAGGT$ GCCTCGCCGAACCTGTGGTGGCAGTTCGTGGCCAGCTTTTCCGAGGCCGCCAAGACGCAGGGC ATGTTCACCACCACCTGCTCAACGACAAGGACTCGATCGCGACCCAGATTTCATACAAGCTC GGTCTAAAGGGCCCCGCGGTCACCTTGTTCACCGGCTGTTCCACCTCGCTGGTAGCCGTTGAC 15 ACTCTCCCCGATAAGGCCGGCTACATCTACGAAAAGGGCATGCTCTTCTCGGCCGACGGCCAT 20 $\tt CTCAAGCCGTTGGACGGGGCCCTGCGCGACGGGGGCCCGATCCATGCGGTGATCAAGGGCTGC$ 10 GCCACCAACAACGACGGCGACCGCAAAGCCGGCTACACGAGCGTCAGCGCCCAAGGCCAGGCC GAGGTGATCCGCTCGGCCCAGATCCTGGCCGACGTGGCGCCCCGAATCCATCAGCTACGTGGAA 25 GCCAGCGACAAGAACGGATTTTGCGGCATCGGGTCGGTCAAGACCAACCTCGGTCACCTGATG GCGGCGGCGGGATGGCCGGCCTGATCAAGACGGTTCTGGCGATGAAGCACCGCCAATTGCCG 15 CCATCGCTGCACTGCGACGAAGTGAACCCCGACCTGGAGTTGGAGCGCAGTCCGTTCTACATC 30 GGGATCGGCGGAACCAACGCTCACGTCATCCTGGAGGAGCCGCCGACGCGCGAGAGCGGCACG 20 GCCGATAACCTGGCCGACTACCTGGAGCGCCATCCCGAGGCCCACCTCAGCGACGTGGCCTAT 35 TCCCTCCAGACCGGCCGCGCGCTTCTGGCCTGGCGGCGCACGGTCCTATGCGAGTACCGCGAG GACGCGGTGACCAGTCTGCGCGAGCGACAGGCCAAGCGCGTCCAGACAAGTCGCGTCCGCTGG ${\tt GACCACAAGGACGTGGTCTTCATGTTTCCCGGTCAGGGCGCCCCAGTACCTCAACATGGGCCGC}$ GACTTATACGTCATGGAGCCGGTCTTCCGCGAGGTCATGGACCGCTGCTTCGAGTTGCTGGCC 40 25 CACCGGACTGATTACACCCAGCCGATCGTGTTCTGCTTCGAGTACGCCCTCGCCCATTTGCTG $\tt CTCTCCTGGGGATTGAAGCCGGCCGACCATCGGCTACAGCTTCGGCGAGTACGTTTCTGCC$ 45 TGCCTCGCCGGCGTCTTCTCCCTGGAAGATGCGATCCGTCTGGTGACCGAGCGCGGTCGGCTG ATGGCGGCTTTGCCCGCGGGCGCCATGCTCAGCGTCCCGGATGCCGAATGCGAGCTGCTGCGG 30

TCCTGCATTGTGGCCGGCGAGCAGGCCGCCATCTCGGCCTTCGAATCGATGCTTCGCAAGAAG CGTCTGTTGACCATGCGGGTCGCGGTCAGCCACGCCGCTCATTCGCAGGTCATGACCGGCGCG 10 ACCGACGCCCTGCGCAGCATCCTGCGGAAGATCCCCCTCTCCGCGCCGACAATTCCCTTCATT TCCTGCGTCACCGGCACCTGGATCACTGCACAGCAGGCTACGGATCGCGAGTATTGGGTGAAC CACATGTGCGGGACGGTGCGGTTCGCGGCGGGTCTGACCGAGCTGGGTCAAAACCGCGAGGCG GTGTTCCTGGAAGTAGGTCCGGGCCGCGACTTGACGTTGCTGGCCCACCGCATCCTGGCCGAC 15 AGCGCGGCCGTGTTCGAGCTGGTCAAGGCGCCCGACGGCGGCGACGACGATGGGTTCCTCCTG CTGGATCGATTGGCCAAGCTCTGGAGGCTGGGGATTTCGATTGACTGGGCCGGCTTCTACGCG GATGAGCGGCGGCGGAAACTCTCGCTGCCGGGATATCCGTTCGAGCGGCGGCGCTTCTGGATC 20 GAGGCAACCCGCTGGAGATCGCCGCCGGCAGGCCCAATGTCCAGGGGCCGCTGGTCAAGGCG 10 ACAACGGCGGCGGCGCCGTCACGGCGGAGCAGGCACGCGTCGTGACCGAGCTACGGGCG ${\tt GGATGCGCGTCGGCCGGCTTGGGCAGCGGGCCTGCGGACTGAATGGCGGTGCCCCGTCCGAG}$ 25 15 30 ${\tt GGCGAGAAGCTTTACCTGGTGGCTTCCGGCTTCGAGCGCCTGGCCGAGACCCGCTTC}$ $\tt CGCCTCGATCCCGGGGCCAAGTCCGATCACCGCCTGCTTTTCAAGGCGCTCGACGAGGCCGAC$ ATCCTGCCGACCCACCTCCTCGACTTCCGCTCGCTTGACTGCGGCGGGCCCGACGCCGACCCC ATGGACCAGGCCGGCTTCTTCGGGCTGTTGCACCTGGTCCAGGCGATGGCAGAGGCCGGCTAC 20 35 AGCCATCCCATTCGGCTGCTGATCGTCAGTTGCGGCGTCTACGATGTCACCGGTGCCGAACCG CTGCAGCCGGCGCGCCACGATGATCGGACCGGCTCTGTGCATCCCGCAACAGTATCCGCAC CTCGAAACGAGCCATGTGGATTTGGGCGTGGTCCATGCCGACGAGCTCCACGCCGCGCGCCAG 40 CGACACCGCTGGCTGGACTACGAGCCAGTCCGCTTGCCGCCGCTCGACCCGGGCCGTCTG 25 CCCTGGCGCCAGCGCGGGTCTACTTGATCACCGGCGGTTTGGGCGGGATCGGCCGCATCCTG GCCGAACACCTGGCCGCACGACCTCGGCTCGCCTGATCGGCCGCGAAACCCTGCCC 45 CTGCTGCACAAGATCCGCGCGATTCGCGATCTGGAAGCGCTAGGCGCCGAAGTCCTGGTCCTC GCCGCCGACGTCGCCAACGAAGCCGCCATGCGCGAGGCCTACGATCGCGCCGAATCCCACTTC

PCT/US99/23535

121

WO 00/22139

GGCACAATCCACGGGGTGATTCACGGCGCCGGCCTGATGGACGCGCAAAGCTTCTCACTGATC GACGCCCTCGACCACGACCTCTGCGCCCGCCAGTTCGAAGCAAAAATCCGCGGCGTCTGCGTG 10 GTGCTCGGCGGCCTGGGCTATTTCGGTTACGCCGCGGCCAACGCCTTCCTCGACGCCTTCGCC CAGGCGCGCAGCCGCGACGCCGCTTTCCCCTGGCTTAGCGTGGCCTGGAGCGATTGGAAGTAC 15 GCCGAGGCTTCGAAGCCGTCACCCGCGTCTTGGCTTGGGGCAAGGCGCCCCACATCGCCAAC TCGCCCGGTGACCTCGGTCGCCGGCGGGATCAATGGGTCAAACTGGCCAGCCTGAAATCGGCG 20 CCGCGCAACGTGGTCGAAGAGAAGCTGGTCGCCATTTTCGAGCAGGTGTTCGGCACTGCGGCA 10 CTGGGCATCGAGGACAACTTCTTTGAGTTGCGCGGGGACTCGCTCAAGGCGGTCATGACCGCG GCCCGTATTCAAAAGGAGCTGAACGTGGAAGTGCCGCTGCCGACCTTCTTCCAGATGCCCACG GTCGCTGGCCTGGCCCAGTTCGTGACGCAAGCCAAGCGCAGCGGCCGGGAGACGATTCGGCGC 25 ACCGCGCGCGCCCACATTACCCGCTCTCGGCTGCCCAGGGCCGCCATTACCTGCACTACCGC 15 ATGGACCCGCGTTGTACCGCATACAACGATCCCTTCGCCAACCTGATCGAGGGTCCGCTGGAC GTGGATCGCGTGGAGCGCATCCTGCACACCCTCATCCTACGCCACGACTGCTTCCGCACCTCG TTCCACTTCCGCGAGGGCGAGCCGGTCCAGGTGATTCACGATCGGGTGGACTTCAACCTGGCG 30 ${\tt CGGATTACCTGCGCGCCCGAGGATTTGCCCGAACGGATGCGCGATTTCATCCGCTCCTTCGAT}$ 20 35 GCGGCGCTCTACCGCGGGGGAGATCCTGCCCGAGCTGGAACTCGAGTACAAGGATTTCGCGGTG TGGCAGCATGAGAACCGGGGCCGCCGCCCAACAGCGACCAGGCCCGCTACTGGACCGAGCAG TTGGCCAATGCGCCCGGGCCGATCGAGCTAACCACCGATTTCCCCCGTCCCAGTCGACGCAGC TTCCGCGGCGACCGCGGGCCGGACCGTGCTTGATGCGGAGCTCGTTGCTCGACTCAAAGAGCAC 40 25 AAGCTCTCCGACTCGCACGACATCGTCATCGGTTCGCCCGTCGCGGGCCGCACCCGGAGCGAA 45 CATACCGCACGGGTCTTCTTGGAGCAGGTCCACCAGACAACCTTGGCGGCCCTCAGCTACCAG GAGCACCCTTTTGACGAAATGGTGGCGACGCTCGGGTTCGCCGCCGATCCGGCTCGCAACCCG ATCTTCGACACGATGTTCTTGCTGCAGAACATGGCCATGGGTGCAACCACCATTCCCGGTCTG 30

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CGGCTCTCGCCTCACGACACTTTTCACCGCAAGGCATTGTGCGACCTGATGCTACAGGCGACC
GAGTATGACTGCCACCTGGAGCTGGTGCTCGAGTTCGCCACCGACCTGTTCCGGCTGGAAACC
GCGCAAGTCTTGCTCGACCGCTACCGCCAAGTCTTGGAGTGGCTGTTGGCGTACCCCCATGAA
TCGATAGACGATTTGACGCTCGCCGGCCACTTTCGCGAAGTCGAAGTGACGATGTCGGACGAG
GGCGACTTTGATTTCTCAGATTTCGAACCCCGCAACGTGAGAAACCTATGGCGCGCC

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(2) peptide sequence

Seq ID No 58 (>pEPOcos6_ORF9.pep)

MKLNVVANRLFDPESPERTEPAKSLLLAVTKVLPQEVPNVRTRAISVDLDRSFDAAAPAWAAS LLVECGAPVEETVVTYHGAARWLRRFDRVAVNGLGPFHPDQPAPLLRERGVYLITGGLGGVAG QLARYLARACRARLVLTARRPLPERDQWDRESAVLSWDDKTRQRIELVRELERLGAEVLVVAA DVADEAAMAQAIEASLARFDALDGLIHGAGIVRVASGRTPIGSMTRAMCEEQLRPKMLGLDVV DRLLRDRRLDFRIAISSLAPILGGLGHVAYAAANLYMDAFATRAAAGNAPWIALNLAEWEYEG PATYDERVGRSLKQLELTNEEGIRVFQTVLALAARGPLQQIIISTGDLQARLDKWIHIKSLHR ${\tt RPGPVQLSRRTAAPQGGFGSERAAFEAAFADAWCDFFGVEEVDPNKNFFDLGASSLDFIHLVS}$ RFSKAIEQHVPLEALLEHSTLHDLAAHLAGDANTDASDEARIRQRLQGAKSGDIAIIGMAGRF PLAPDLDTYWRNLVGGIDAVSFFSAEELRAAGVTAAEIHHTNYVPAKGRCADQDLFDAAFFEY TASDAELMDPQNRVLHEVVWHALEDACFDFNGDHGQVGLFAGASPNLWWQFVASFSEAAKTQG MFTTTLLNDKDS1ATQ1SYKLGLKGPAVTLFTGCSTSLVAVDAACRS1WSGQSDMAVAGAVSL TLPDKAGYIYEKGMLFSADGHCRAFDANATGMVFGDGAGAIVLKPLDAALRDGDPIHAVIKGC ATNNDGDRKAGYTSVSAQGQAEVIRSAQILADVAPESISYVEAHGTGTKLGDSIEIKALKQAF ASDKNGFCG1GSVKTNLGHLMAAAGMAGL1KTVLAMKHRQLPPSLHCDEVNPDLELERSPFY1 NTRLRDWVAPGGPLRAGVSSFGIGGTNAHVILEEPPTRESGTRMRHWKLLMLSAASEAALDRQ ADNLADYLERHPEAHLSDVAYSLQTGRRVLAWRRTVLCEYREDAVTSLRERQAKRVQTSRVRW DHKDVVFMFPGQGAQYLNMGRDLYVMEPVFREVMDRCFELLAPLWSEHPRQILYPEGGVSTLL ${\tt HRTDYTQPIVFCFEYALAHLLLSWGLKPAATIGYSFGEYVSACLAGVFSLEDAIRLVTERGRL}$ MAALPAGAMLSVPVPECELLRLLDGFHAQSAAHLALAVDNGASCIVAGEQAAISAFESMLRKK RLLTMRVAVSHAAHSQVMTGATDALRSILRKIPLSAPTIPFISCVTGTWITAQQATDREYWVN

HMCGTVRFAAGLTELGQNREAVFLEVGPGRDLTLLAHRILADSAAVFELVKAPDGGDDDGFLL

LDRLAKLWRLGISIDWAGFYADERRRKLSLPGYPFERRRFWIEGNPLEIAAGRPNVQGPLVKA

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SDIGAWFYVPQWRRSVLAEPGTTAAGAAVTAEQARVVTELRAGCASAGLGSGACGLNGGAPSE RPKESVAPAGSTSAAAQTGADCPTPTGEPAAVPKDGAEPRPTWLIFADAGGLAESFAKRVQAR GEKLYLVASGSRFERLAETRFRLDPGAKSDHRLLFKALDEADILPTHLLDFRSLDCGGPDADP MDQAGFFGLLHLVQAMAEAGYSHPIRLLIVSCGVYDVTGAEPLQPARATMIGPALCIPQQYPH LETSHVDLGVVHADELHAARQLDSLLAECLSATAERQLALRGRHRWLLDYEPVRLPPLDPGRL PWRQRGVYLITGGLGGIGRILAEHLARTTSARLVLIGRETLPDRDDWDAWLNRPQPVDATHER LLHKIRAIRDLEALGAEVLVLAADVANEAAMREAYDRAESHFGTIHGVIHGAGLMDAQSFSLI DALDHDLCARQFEAKIRGVCVLDRVLADRTLDFCLLMSS1STVLGGLGYFGYAAANAFLDAFA QARSRDAAFPWLSVAWSDWKYWTERKMDNEVGAVIDSLSMEPAEGFEAVTRVLAWGKAPHIAN 10 SPGDLGRRRDQWVKLASLKSAHSSEPEPARHGRPALSSEWVAPRNVVEEKLVAIFEQVFGTAA ${\tt LGIEDNFFELRGDSLKAVMTAARIQKELNVEVPLPTFFQMPTVAGLAQFVTQAKRSGRETIRR}$ TAPRPHYPLSAAQGRHYLHYRMDPRCTAYNDPFANLIEGPLDVDRVERILHTLILRHDCFRTS FHFREGEPVQVIHDRVDFNLARITCAPEDLPERMRDFIRSFDLERPPAMRAGLFVTGPERHVL LIDFHHIITDGVSFENFVGEFAALYRGEILPELELEYKDFAVWQHENRGRRANSDQARYWTEQ ${\tt LANAPGPIELTTDFPRPSRRSFRGDRVRTVLDAELVARLKEHAARLGITLYSLLLGGFSLLQH}$ KLSDSHDIVIGSPVAGRTRSELQDLLGAFVNTLPMRHRIDPTHTARVFLEQVHQTTLAALSYQ EHPFDEMVATLGFAADPARNPIFDTMFLLQNMAMGATTIPGLRLSPHDTFHRKALCDLMLQAT EYDCHLELVLEFATDLFRLETAQVLLDRYRQVLEWLLAYPHESIDDLTLAGHFREVEVTMSDE GDFDFSDFEPRNVRNLWRA

pEPOcos6_ORF10 sequences:

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(1) nucleotide sequence

Seq ID No 59 (>pEPOcos6_ORF10.seq)

25 ATGGCGCGCTGAGCCGCACAGATCTCCAACTCGCCATTCACCAGCGCACCGTGGAGCGCAA
TATTGGCGCGCTCTGTTCGAGCGCCATCCGCAACGGTCCAGTTTGCCGGGGGTGCTCACCGCC
CCGATCGGCGACGAGCCCGCGAGACCTTGTCATTCGTCCTCGACGAAGATCCCCTTCGG
CTGAGTAATCGTTCGCCGCAACGCCTGCTCACGGTGTTGGCGGCTGGCGCTCGCGGCTTTCCTC
CACCGCTGCGACGGCGTGAGCGCTTCACCCTGGGGTTGGCCCTACCGCGCCAAGCCGATGAC
30 CATCACCCGATCCTCAACAGCTTGATCGCGCTGGGGGTCGACTCGAGTACGACCTTC

CGCGATCTGCTCTATGCGCTTCGATCCGAATACCACGAGGCGATGCGCCACGCCAACTTTCCG $\tt CTGGCGACCTGGTGGCGGGCGTACCCGGCGGGAACGGCGCGTTCGACGTCGCCCTCAGCCTG$ 10 GACCCCTTCACAGACGCGATTCGCTGGAAGACCACGCGATCGGCGCGTTGTTCCGGTTCGCA ${\tt TTGGAGGGTGAGCGCCTCACCTGCCGATTGCGATTCGACCCTGCGCGCTATGACCGTCCCGCG}$ ATCGAAAACCTCGCCGATCGTTTCGCCCGCTTCCTCACGCGCCTGTGCCGGGACGCCTCCACC GTCATCCAGGCGCTGGACCT'ITCGCTGCCAAGCGATGAATCGGTGTGGCGCGTCACTGAAGGC 15 ACGCCCGATCAGCCGGCGATCACGTTGAACGGGGACGTCCAGAGCTACGCCGAGGTCGACCGC CGCAGCGACGCGCTGGCCCACCTCCGTCGCCACGGCGTCGGTCCGGAAACGATTGTGGCC 20 GTCAACGCCCGGCGCGCCTAATCAGCTGACGGCCCTGCTCGCGGTCCATAAGGCCGGCGGC 1.0 GCCTACCTGCCGATCGATGCCGAGGAGCCGGCTGCCCGCCAGCAATTCAAGGTGCGCGACAGC GGGGCGCGCTTGGCACCTGGAGCCGTCGCCGGACCAGGCGCTGACCGTCACCGACCTGCCGCGG 25 TCGCTCAATCCGGCCTATGTGATGTACACGTCCGGCTCGACCGGACAGCCCAAGGGTGTGGTG 15 GTTCCCCACCGCGGGGGTCAATCGTTTGAATTGGGGGCAGTCCCGTTTCCCGCTGGACGAA CGCGACCGAATCCTCCAAAAGACGCCGCTGCTGTTCGACGTGTCGGTCTACGAGCTGTTCTGG GGCGCATGGAGCGGGGCCACCCTGGACATCCTCGAGCCCGGCGCGCGAGCGCGACCCCGACGCA 30 GTGGCCAGGGCCCTGGCCGAGCGCGCCATTACCGTATGCCATTTCGTGCCTTCGATGCTGCTC GTCTACTTGGAAGTCATGCGGCGCCACCATGCGCCGCCCGTGCCGGACCGGCTCCGTTACGTC TTCGTCAGTGGCGAGGCCCTCGAACCGGACCACCTCGCCGGGCTCCAGCAGATTGGTCGGCGC 20 35 TGCTTCGCCTGTCCCGCCGACCATGTGCCGCGCGGGATCCCCATCGGGCAGCCGATCGACAAC GTCGCACTGCACGTTCTCGACCGGCGCGGCCGTCGCCAGCCGCCCTATCTTCCTGGCGAGCTG TTCCTGGCCGGCGACTGCCTGGCGCGCGCTACCTCAACCGTCCCGACCTGACCGCGCTCCAC 40 25 TTCGTGCCCAATCCCTTCGGCAACGGCGAGCGCATGTACCACAGCGGCGACTTGGCGCTCGTG CGCGGCGACGGCCAAGTGGCGTTTCTCGGCCGCCGTGACCACCAAATCAAAATCCGTGGTCAA $\tt CGGGTCGAACTGGGCGAAATCGAGGGTCATTTGCGCGGGGCTCGAAGGCATCGCCGCCGCCGTC$ 45 GTCCAGGCCGAGTCGCAGCACCATGAAACCCTGCTGCACGCCTACGTCGTCACCAACGACGCG GGCCTCAATGCGGCCCGGCTGCGCCCCCCCCCCAACATCTGCCCGAGTACATGATTCCC 30

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CTCGCGCAACGTGCAACGCCGCTCGCCAGCGGCGCCCTTCGTGGAACCCAGCGGGCCCACC
CAGCAGCGTATCGCAGAACTGTGGCGCCAGGTCTTAGCGGTCGCCGAAGTCGGCGCCGAGGAT
CCCTTCTTCAGCATCGGCGGCAACTCGCTCAATGTGCTCAAGCTCAGCGCCGCGCTGAGCGAC
GCCTTCGCGCGTGACATTCCCATGCCGGCCCTGTTCCAATACGACACCATCGCCGCCCAGGCC
TCCTGGCTCGACGGCAGGTTGACGAACGGGCCCAATCCGCCGCGCTCGACCGCCAGGCCC
GAGGCGGCGCTGACCCTTCAAGAGACCGTCGCCATTTTTGAGGGATTCGATGACGAACCA

(2) peptide sequence

Seq ID No 60 (>pEPOcos6_ORF10.pep)

MARLSRTDLQLAIHQRTVEREYWRALFERHPQRSSLPGVLTAPIGDESTRETLSFVLDEDPLR
LSNRSPQRLLTVLAAGLAAFLHRCDGAERFTLGLALPRQADDHHPILNSLIALGVAVDSSTTF
RDLLYALRSEYHEAMRHANFPLATWWRGLPGGTAPFDVALSLDPFTDGDSLEDHAIGALFRFA
LEGERLTCRLRFDPARYDRPAIENLADRFARFLTRLCRDASTVIQALDLSLPSDESVWRVTEG
VRRGYSQDLTLDRAFRRQAAQTPDQPAITLNGDVQSYAEVDRRSDALARHLRRHGVGPETIVA
VNARRGPNQLTALLAVHKAGGAYLPIDAEEPAARQQFKVRDSGARLALEPSPDQALTVTDLPR
LFLDDASLFADGGLDVPRGADSLNPAYVMYTSGSTGQPKGVVVPHRGVVNRLNWGQSRFPLDE
RDRILQKTPLLFDVSVYELFWGAWSGATLDILEPGAERDPDAVARALAERAITVCHFVPSMLL
VYLEVMRRHHAPPVPDRLRYVFVSGEALEPDHLAGLQQIGRRLGRTIPLVNLYGPTEASIEVS
CFACPADHVPRRIPIGQPIDNVALHVLDRRGRRQPPYLPGELFLAGDCLARGYLNRPDLTALH
FVPNPFGNGERMYHSGDLALVRGDGQVAFLGRRDHQIKIRGQRVELGEIESHLRGLEGIAAAV
VQAESQHHETLLHAYVVTNDAGLNAARLRAALAQHLPEYMIPQRFSRLAELPLLAAGKIDRAA
LAQRATPLASGAPFVEPSGPTQQRIAELWRQVLAVAEVGAEDPFFSIGGNSLNVLKLSAALSD

AFARDIPMPALFQYDTIAAQASWLDGQVDERAQSAALDRQAAEAALTLQETVAIFEGFDDEP

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PCT/US99/23535

pEPOcos6 ORF11 sequences:

(1) nucleotide sequence

Seq ID No 61 (>pEPOcos6_ORF11.seq)

ATGACGAACCATGACCATCACGAGGAGGAGCAGCGGCCTGGAGATCGCCGTCATCAGCATGGCC TGCCGATTCCCGGGTGCTATGGCCTGCCGATTCCCGGGTGCTGCCGATTGCGACGCATTCTGG GAAAACCTGATCAACGGGACCTCCTCGATCACCCATTTCAGCGACGACGAGCTGATCGCGGCC GAACGGTTCGACGCGGCCTTCTTTGGGTACTCCCAGCGTGAGGCCGAGCTGATGGACCCCCAG 10 $\tt TTCCGCCTGCTCCATGAATGCGCCTGGTCCTGTCTGGAACAGGCCGGCATCGATCCGCGCGTC$ GAAGCCGCGCCGATCGGGCTGTAT3CCGGCGCGACGACACACCTACTGGAACGCGCTCTCG TCGCTCGACCGGGGCTCGGCCGAATCGGAGCAATTCGCCGCCGAACAACTTTGCAACCGCGAT TTTCTGTGCACGCTGGTCGCCGCCGCGCTCAACCTGAAAGGCCCCGCGGTGGTGGTTCAAAGC GCCTGTTCGACCTCGCTGTTGGCGGTCCACTCGGCCTGTCGTGCGCCTCCTGACCGGCGAATGC CGAGTGGCCTTGGCCGGTGGGGTGCGCTTCCCACGCCCGAGCGGTTATCGCTACGAA $\verb|CCTGGCATGATCTTCTCGCCCGACGGGGTGTGCCGGCCGTTCGACGCGGGCGCTAACGGGACG|\\$ GTGCCCGGCGAAGGCGCGGGGCTGGTAGCGTTGAAGACGTGCCCTCCAGGACGGC GACACGATCCACGCCGTGATTCGCGCGACCGCGGCAAACAACGATGGTGCCCGCAAGACCGGG TTCACCGCGCCCAGGCCCAAGCCGAAGTCATTCGCACGGCGCTGCGCCTGGCCCGG $\tt GTGCCGGCCGAATCGATCGACTCGAGGCCCACGGGAACCGGCACGCCGCTAGGCGACCCG$ 20 ATCGAGGTAGCCGGCTTGGTGGAGGCCTTCGCCAGCGAGAAGCGCGGCTATTGCCGGCTGGGC TCGGTCAAATCCAACCTTGGTCATCTGGACACTGCTGCCGGCATCGCCGGCCTGATCAAGACC GTGCTGGCGCTCGAGCACGCGCACATCCCCAAGTCCTGCCACGTCGCCACGCCCAACCCCGCG GCGCGCCTACACAAGACGCCTTTCCGCATTGCCGCCGACGGGATGGCCTGGCCGCGGCGTATG 25 GCGACGCCGCGGCGGCGGCGGTGAGTTCGTTCGGCATCGGCGCACCAACGTCCACGCGATT TTGGAGGAGGCGCCCCCGCGCGCCCGAGCTGGCGGACGGGCGCAGTCAGGTGTTCGTCTTC TCCGCCAAGGACGAGGCGCGCTGGACCGTGCCCTTGCCAACTATGGTGCGGCCTTGGAGAAG CGCGGCGACCTCGCGGCGGGCGCGGTGGCCTGGACGCTCCAAAACGGCCGGGCCGCATTCGAA

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GGGCAGGGGAGCCAGTACCGTGGCATGGGCCACGACCTGTACCGCGAAGAGCCGCGTTTCCGG 10 ${\tt TTGCTGGGCTACCGGACGAGGACGAGCCAACCGACCAGATCGGGACGTCCTCGCAGGGCCCG}$ AGCCGGTCAGCCGCATCGAACCCAGCGGAGCTCCTCGACAGCACCGAATTCGCCCAACCTTTG ${\tt ATGATCGGGCAGCCTGGGCGAGTACAGTGCTGCATGTATTGCAGATTTCTATGCACTCGAT}$ 15 ${\tt CAGGTGCTGCCCTTCATTCTGACCCGCGGTCGAGTCATGGCGCAATTGCGGCGCGGCTCGATG}$ $\tt TTGGCCGTCAGCGGTGACAGCGTTCTGATGCGCGAGCTGATCGCCGATGCGCTCGATTTGGCG$ GCGATCAACGGCGCTGACCAATTTGTCTGGAGCGGGCCGAGCCGAGGCTGTCCAAGCCGCGGG 20 GTCCGACTGCGCGGCCGGCCTGCGTGCCACCGAGCTGAACACCTCACACGCGTTCCATTCA 10 GCCATGATGGATCCCATTCTGGAGGAGCTAACGGTTGCCGGTTCGCGACTTCAGGTCGGTGTC ${\tt GGGACGATTCCGGTCGTTTCATGCGTTACCGGAACCTGGTTGACGGCGAAGCAGCTGGCCGAT}$ 25 CGCGAGCATTCGAATGCCCGCCTCCCGGTCGTCACCAGCCTGCGCCACGCTCGCCAGGCGACG 15 $\tt CCCGATCGCCAATACCTGCTCGAAACGCTCGGCTGCCTTTGGCGACACGGGGTTTCCGTCGAT$ 30 TGGGGGCCCATGCCGGACGTTCGCGACGCTTGGTTTCGCTGCCCGGCTATCCCTTTTCCGGC CCGTCGGGAACGCGCCAACTCAGCGCCGACGCGCGACCTCCCGAACACTCCGGAGCCGACA 20 ${\tt TCCGGCGCCGTGTCGGCGATCAAAGCGCCAATCGCCGCCGATCCCGGCCTCTATCGCCTC}$ 35 TCCTGGCGCCAGGCCGGAACGGCGCCGCTCGGTCCGCCCGATCTCGGTCCGCCCCGCGACTGG ATCGTCTTCGCCTCTGATTCTCACCTGCTCCAGGCGCTCAGGGCCAATCTCGGGACGCGCGCT CAGCGGGTGACGCTGGTGACGCCGGGCCAGGAGTACGCAGCCGAGCCGTCCGGGTTTCGGCTG $\tt CGGCCGGACCAGATCGACGATTACCGCGCCCTGTGGGCGGACTTGGCGCAAACCGGTATTGTG$ 40 . ACCCTGGACGAAGTGCGCGAGGGCGGCTTCCTGCCCCTGACCCGCTTGATCCAGACTCGCCCG CCAGGCGGACCGAGCGGACTTCTAAGCCTCACGATCGTCACCCCGGCCGCCCCTGGCGCTGGGC 45 GACGAAGCGACGCCCCGGAATGGGCAATCCTGCACGGGATGGTCGCCGGCTTAAGCCGCGAT TATCCCGAATGGCGCTTCGTCTCGATCGACGGCGGCGACCCATCCCCGCATCGGTGCGAAGGT

ATGTGGCGCGAGGGTGTGTGTACATGATAACGGGCGGATTCGGCGGGATCGGTCTGGCGCTG 10 GCCCGCGCCCTGGCTCGAGAAGCTCGCCCAAGCTGATCCTGGTCGGCCGAAACCTGCCCACC CCGCCGATCGATCTCGAGGCTTGGGACGCCGCCGCTTGATTCTCACCGCCGACGTCGCCGAC CAAGAGGCCATGCGCCGCGTCTTCGATGCCGCGCACGCCCGGTTCGGCGCCATCGACGGCATT 15 GACGTGCTGCACGCCAAGGTTCGCGGTACCCTCGTGCTGCAAGGCCTGAGGGCAATCGATGCG CCGCTGTTGCTGATGTCCTCGCTGGACGCCTGGCTTCCCGGTCCCGGTCAGACCGCCTATGCC GCCGCCAACGCCTTCCTCGACGCCTTCGCCAGTCTGCGCCGGCGAGAGGGGAGAGCCGGTGTAC 20 1 C AGCGTTGGCTGGGACAGTTGGTGCGAGGTGGGCATGGCTGCTCGGGTCGCTGCCCGATCGGCC GACGAACGCGGCCGCGCGCGAGGGGATCAGCCCTCGCCAGGGTTGGCAGGCTTTGAGC CACAGTCGATCCAGCCCTACGCCGGTCGCCTCGAGCGAACCCGAGGTGGCGCTGCCGCGCTGG 25 ACCGCATCCGCCTGCCAAGCCGTCATCGAGCGTGTTTGGTGCGAGCACTTCGCCACCGCCGCC GTGCCTCCCGATGGCAACTTTTTCGAGCTCGGCGCCAGTTCCTTCGACATCGTCCAGCTCAGC 15 GCTCGACTTCAACAACAGTTCGGCCGAGATGTCAGCCACACCGTGCTCTACAGTCATCCCACC 30 GTCGCCTTGCTGGCCGGCTACTTCGCCAATGACCCGACGCCGTCCGGTGCTGCCGACGAA CGCGACGAAGCGGTGCGTCGCGGCCGCGACCTCTTGAAGAGCCGCCGGCGAGGAGTA 20 (2) peptide sequence 35

Seq ID No 62 (>pEPOcos6_ORF11.pep) MTNHDHHEESSGLEIAVISMACRFPGAADCDAFWENLINGTSSITHFSDDELIAAGVDARDLT PQYVRAAGQIDDAERFDAAFFGYSQREAELMDPQFRLLHECAWSCLEQAGIDPRVEAAPIGLY AGAADNTYWNALSSLDRGSAESEQFAAEQLCNRDFLCTLVAAALNLKGPAVVVQSACSTSLLA VHSACRALLTGECRVALAGGVALRFPRPSGYRYEPGMIFSPDGVCRPFDAGANGTVPGEGAGL VALKTLKRALQDGDTIHAVIRATAANNDGARKTGFTAPSAHGQAEVIRTALRLARVPAESIDY VEAHGTGTPLGDPIEVAGLVEAFASEKRGYCRLGSVKSNLGHLDTAAGIAGLIKTVLALEHAH IPKSCHVATPNPAARLHKTPFRIAADGMAWPRRMATPRRAAVSSFGIGGTNVHAILEEAPPRA PELADGRSQVFVFSAKDEAALDRALANYGAALEKRGDLAAGAVAWTLQNGRAAFEWRASAVAS DLDELAGALRGERPGAVKKNRMAREDKPVAFLCSGQGSQYRGMGHDLYREEPRFRHHLDACLA

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ILAEHKPEIDWLALLGYRDEDEPTDQIGTSSQGPSRSAASNPAELLDSTEFAQPLLFSMSYAL GRLWLDWGVRPTAMIGHSLGEYSAACIADFYALDQVLPFILTRGRVMAQLRRGSMLAVSGDSV LMRELIADALDLAAINGADQFVWSGPSEAVQAAGVRLRGAGLRATELNTSHAFHSAMMDPILE ELTVAGSRLQVGVGT1PVVSCVTGTWLTAKQLADPRYHARHAREPVRFAAGLATLTGEEPPLM LEVGPGSTLAALAREHSNARLPVVTSLRHARQATPDRQYLLETLGCLWRHGVSVDWGAHAGRS RRLVSLPGYPFSGAVRRLAGDPLRLLAGARAVAAPSGTRQLSADARDLPNTPEPTSGAVSAIK APIAAADPGLYRLSWRQAGTAPLGPPDLGPPRDWIVFASDSHLLQALRANLGTRAQRVTLVTP GQEYAAEPSGFRLRPDQIDDYRALWADLAQTGIVPRYIAFLAPFMYRARMAGDASTLDEVREG GFLPLTRLIQTRPPGGPSGLLSLTIVTPAALALGDEATRPEWAILHGMVAGLSRDYPEWRFVS IDGGDPSPHRCEGLARLIALHAVDEAGPTRLALRGLHAWVPQCEHVQPATIPGAGMWREGGVY MITGGFGGIGLALARALAREARAKLILVGRNLPTAPIDLEAWDAPPLILTADVADEEAMRRVF DAAHARFGAIDGILHAAGVPGGSLFANQSDAAFEDVLHAKVRGTLVLQGLRAIDAPLLLMSSL DAWLPGPGQTAYAAANAFLDAFASLRRREGEPVYSVGWDSWCEVGMAARVAARSADERGRLAR EGISPRQGWQALSRALALDPPHLMISRTDLTSRWHSRSSPTPVASSEPEVALPRWTASACQAV IERVWCEHFATAAVPPDGNFFELGASSFDIVQLSARLQQQFGRDVSHTVLYSHPTVALLAGYF ANDPTPSGAAADERDEAVRRGRDLLKSRRRGV

pEPOcos6 ORF12 sequences:

(1) nucleotide sequence Seq ID No 63 (>pEPOcos6 ORF12.seg) GGCGCTGCCGACGTGGCCGCCTTCTGGCGCAACCTGGTCGAGGCCAAGGAGAGCGTGCGCTTC TTCGAGGACCACGAGCTGCGGGGCCGCGGCGTGCCCGAGGAGATCTTGCGCCTGCCCAACTAC 25 GTGAAGGCCAAGCCACTGCTCGCTGATGGCGAAGCTTTCGACGCGGACTTCTTCGGGTTCCAT CCGCGCGAGGCCGCCTACCTGGACCCGCAAGTTCGGCTCCTGCACGAATGTTGTTGGACCGCG TCCAGCAATCTCTCGTTCCTGTTCGACCGCATCGATCCGCGCGACTCCCCCCTGCAGAAGCGC

TATGTGGCCGAGCTGAACGCGGCCTCCTTCGCCACCCAGATCGCCTACCGGCTCGATCTGAAG 30 GGGCCGGCCATTTCGATTCAAACCGCCTGTTCGACGTCACTGGTGGCGATTCACCTGGCGGCG

AAAAAGCCCGGCTATCTCTACCGCGAAGGCTACATCAACTCGCCGGACGGCCACTGCCGGGCC 10 TTCGACGCCGACGCGGCCGCCACCATCTTCGGCGACGGCGTCGGCATCGTCCTGCTCAAACGC TACCGCGACGCCCTACGCGACGGCGATCACGTGTACGCAGTGATCAAAGGCTCGGCGATCAAC AGTGACGGCCATCGCAAGGTGTCCTACACGGCGCCGGGCAAGAGCGGTCAAGTGGCGGTGATC CGCGCTGCGCTGGCGGCCCCAGGTAGAGCCGCAAACCATTCGCTTCGTCGAGGCCCACGGG 15 ${\tt ACCGGCACACTCGCCGGCGATCCGATCGAGGTAGAGGCGTTGACGGAGGTCTTTGCCGAAGCG}$ GGTCGCGGTACCTGCGCCCTGGGTTCGGTGAAGACCAACATCGGCCACTTGGATGTGGCGGCG ${\tt GGCGTGGCCGGTTTCATCAAGGCGGTCTTGGCGCTCGAGCGGCGCGTCCTCCCGCCCAGCCTT}$ 20 10 ${\tt CACTTCGTCCGGCCCAACCCGGCCATCGATTTCAACGGGCCCTTCTACGTTTGTCGCCAAATCCGCCCAAATCCGCCCAACCCGGCCCAACCCGGCCCAACCCGGCCCAACCCGGCCCAAATCCGCCCCAAATCCGCCCCAAATCCGCCCCAAATCCAAATCCGCCCCAAATCAAATCCAAATCCAAATCCAAATCCAAATCCAAATCCAAATCCAAATCCAAATCCAAATCCAAATCAAATCCAAATCCAAATCCAAATCAAATCCAAATCAAATCCAAATCAAAATCAAATCAAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAATCAAAATCAAAATCAAATCAAATCAAATCAAATCAAAATCAAAATCAAAATCAAAATCAAAATCAAAATCAAAATCAAAATCAAAATCAAATCAAAATCAA$ GAGCGGTTGACGGAGAACGGGCGGTTGCGGGCCCGGGGTGAGTTCCTTTGGCATTGGCGGCACC CCAGGCGCGAGTCCGTTCCTGTTCCCGCTATCGGCCAAGACGCCGGATGCGCTGGCAGGCCGT 25 TGCCACGACCTTGCCGACCACCTGCGGGCGCACCCCGAGCTCCTCCTGGCCGATGTGGCCCTC ACTCTGCAGATGGGGCGGCGTCGTTCGCCTACCGCCATGTGGTCCAGGCTGCGACGGCGGAG . 15 GAGCTGATTCGCGGTCTGGGAGCGTTCCGACAGGGGTCCATCCGCAAGAGGCGGAATCGAGTA 30 CAATGGGTGTTGGCAGGCGAGGCGATGTCGCTTGACGCCGGTTTGCGGCTGTACGCCGATTGG CCGGTCTATCGGGAGCGGGTCGACGTCTGTCTGGCGATCGTCGCCAAAGCTGCGCCAAATCGAC GGCCGGTCATTCCTACATGAGTGGATCGAGCGACCGCGGGGGTTCCTGCCGAATGGTCGACG 20 35 CAGCGCATGTGGAGCCGTGGGCTGGGCGGACAGGTCGGCGTGGTTTTGGCCGAATCCCTGTCG TTGGAACAAGCGCTGGCGCTGTTTTGTGCCAGACACCGGTTCCCGGCGATGCCACACCTCAG $\tt CGCGAACGCTTGGTTCGGACACTGSAAGGCTGCCGGTTTCGTCCACCACGATTTTTGATTTCG$ ${\tt GCAGACAGCTCGGGTCGACCCCTGGACCTCGCCGAATTCGCTCATGTCGATTTTTGGTGCGGT}$ 40 25 GGCCAAAGCGCCTCGCCCAATGAGGCGGAGCTGCGCTCATGGAGCGACGCCGCGCCCGAGCTG GTGACCTTGGCGATCGGCCCATCCTTTCTCGAGGCCGCCTCCGGGACGGTGGGTCTGGCGATC GACCCCAAGCGACCGATGACCTGTCTTCAGCGCACGGTGGCCGCGTTGTGGGAATGGGGATGT 45 TTCGTGCGGGTAATTCCCACGATCGGCGACCCCCTTCGCGGAGCAGGCGCGCGGAGGATGACTTG

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GAACGCCCACGCGCCCAGTCAAGCATCGCCTCGGCAACCACCACGGCTCCGTCTCATACGTCG GCCAGCGTGGCCGTGGCCACCATTCTCGAAACCGTCCGTGCCTATTTCGGGTTCGCCGCCGTG 10 $\tt CGTTCCACCGACGCCTTCTTCGAATTGGGCGGCTCCTCGCTGGATTTGGTCAACCTGGGCCAG$ GACCAGTTGGCGCTGGCCCTGACATCCGCGGCGCTCAGCGCAGAGGCGCCCCCTTAAGGGGC GGTCATCGCGCATCGACTTCCGGCACAGCCGCGAGCTCGGCCGCCTCCACCGCACCGACGTTC 15 $\tt CCGGGGGACGCTCACTCGCAGCCCAGCTTCGTTCGCGAGCAGGACATCGCCATCATCGGGATG$ GCCTTCCGGGGACCGGCCGACGACCTGGACGCGTTCTGGAACAACCTGGTCGAAGGGGTC GAGTCGATCACCTTCTTCAGCGAGGACGAGCTGCTGGCGGCGGCGTCCCCCGCGAACATCTG 20 10 TTTTTCGGTTATTCGGCGCGCGGGCGGCGGTCATGGACCCGCAGTTCCGCGTGTTCCACGAA TGCTCCTGGCACGCACTGGAGCACGGCGGCTACGATCCGACCCGATGCGCGGCATCGATTGGC GTCTACGCCGGCGTGACCAACCACCTGCCTTGGCTGATGCGAACTTTGCCGCACCTGACCGAG 25 GAGGAGCAATTCGGCGCGCTGCTCCTCACCGACCGCGAGTTTTTCGCACCGCTGCTCTCCTAC AAGGTCGGCCTGCGCGGACCCGCTATTTCGCTGCAAACCGCCTGTTCGACGTCGTTGGTGGCG 30 ACGGCCAGCATCGAGCGCTGCGGCTACTTCCACCAAGAAGGCTACATCCTCTCGCCTGACGGC CTGCTGAAGCCGCTGGCCCAAGCCTTGGCCGACGCGGACACGATCCACGCGGTGATCAAGGGA 20 ATCGGCATCAACAACGACGGCGCGCGCAAGGTCGGCTTCACCGCACCTAGCCGGGCCGGTCAG 35 ACCGAGGCGATTCGGGCCGCGCTGCGCGACGCCGGGGTGGCGTCGAACCGCGTCAGCTACGTG GAGGCGCATGGAACCGCGACCAGAATGGGCGACCCGATCGAGGCCTTGACCCAAGCC TTTCGCGCCGAAGCCGACGGTCCGCTTCCGCCCGGCTCCTGCCTACTCGGCTCGGTGAAGTCC AACGTGGGCCACCTGAACGCCGCGGCCGGCCTGGCTGGTCTGGTAAAAACCGTGCTGGCGCTC 40 CAACACCGCCGCCTGCCGACCAGCCTGTTCTACCAGTCGCCCAATCCACACATCGACTTTGCG 25 GCGAGTCCGTTCCGCGTGAACGGCCAGACTTCGGATTGGGTCGCCCAGAGGGGACGCGGTTG 45 GACGCCGACGGCTAGTGCTGCCGATCTCGGCCCGCACGCCGACCGCCCTGGCGCACATCGCG

GCGATCAAGCTGCTGCGCGCCGTCGTCCACTCCGCGGAGGTGCCGCCAGCTCAGGCGCCGGTC 10 TCGGATGCGCCGCGCTGTGTTTTTTTTTTCCCGGCCAGGGCGCCCAATACCCGAGCATGGCC CGCGACCTGGTTCGAAACTGTCCCGACTTCGCCCTGCACCTGGACCCCTGCCTCGACCAGTTG GCCGAACTGCTTCCCGAAGATCCGCGTTGCATCCTGTTCGGCGATGGCCCCGCCGATCGGCTC GACCAGACGGCCTACACTCAGCCGCTGCTCTTCTCCGTGTCCTACGCCTTGGCGCGCTGGTTG 15 GGCGATTTCGGCATTCGCCCCGATGCGATGATCGGCCACAGCCTGGGCGAATACGTGGCGGCC ATGGGCTCGGCCGCGCGCGGAGCGATGCTGGCCGTCCCCTTGCCCGAATGGGAACTGGAGGAA 20 $\tt CGCCTGGAGCTTCTGGCCGACGACCGAATCAGCATCGCGGCGGTCAACACCGCCGAGAGCTGC$ 10 GTCATCGCGGGACCCAGCGAGGCGATCGAGCGCTGCGCCCAGCGCTGGGCCGCAAGGCCTG ACCTGTACGCCGCTGCGCACGTCCCACGCCTTCCACTCCGCGATGATGGAGCCGATTGTCGAA 25 $\tt CTCSACGGCAAGCCGATCGATTCCGCGGCGGTGATGCAGCCCGACTATTGGGTGCGCCACCTG$ ${\tt CGCCAACCGGTCCGCTTTCACGAGGGACTCAGTCACCTGTTGGCCGAGGACACCCATGCTTGG}$ 15 GTCGAAGTGGGTCCCGGCCGAACCCTGTCCTCCTTCGTCCGCCGCCACCCGGCCTACCGTCAC 30 ${\tt CGAAGACCGGTGGAGCTGGCGCAGCCCGAGCCCGAGGCGGAGCTGGTGAAAAACCCCGATCCC}$ 20 35 ${\tt CAGGCGACCGTTCTGGTCTTCGGCGACGGGTCGAGCTGTGCCGCGCGGCGGCGGTCGCTCAGGTG}$ CAGCGCCAGGGGCTGAAGTGCGTCTCGATCACCGCGGGGCCCCAATTCGCGCGGGAGAGCGAC ATGCGCTTCACGCTTGACCCCGCTGATCCGCGCCCAGCTCGACCAGCTCTTCGCGGCCCTCGAT 40 GGCTCAGGCTCGCGGCCGCGGTACGTCCTGCACCTGCTGACCCTGAACCCGCCCCCGGATGCC GACATCGCGCCTGTCTCGATCACCGTCGTCACCGCGGGGTCGTCGCCGTCGCGGACGAAGCG 45 ATTCGCGAGCCGCTGCAGGCGCTGATCGTGGGCCCGTGCCTGGTCATCCCGCAGGAGTTTCCC GGGCTCAGCGTTCGGCTGGACGTCAACGTCGACGATCCGGCACCGCGTCTGGCGGAGCGG $\tt CTCGTGGCCGAGCTCTCGGGCACGGATCACATGGTGGCGCTGCGCGGCGGCGAGCGCCTAGTG$

. 133

GCCGATGTCGATCAAGTCGATGGCCTCGGTGTGGGGGATCGCCAAGGTGCCCTTGCGCCGCGAG GGCCACTACCTGATTCTCGGCGGCCTGGGCGATATCGGCTACCACTGTGCCCGCTATCTGGCC GAGCGAATGCTGCGCGAGGGAAACCTGGATTCCCGGCAGCGCACGCGCATCGAGCGCGTGTTG TTGGCCGATGTGTTCCGCGAAGCACGGGGCCGATTCGGCGCCCATCGCGGGCGTGATTCACTCG GCGGGGATTCCGGGACACGTCCACTCGATCGACGAGCTGGTGCGCGTCCGCGACGAAGCCCAA TTCACCGCGAAGGTTCGAGGGCTGCACCACCTGGCCGAGGTCGTCGATCCGCTGAACCTCGAC TTTTGTCTGCTGTCTCCTCGACCGTCCTCGGCGGGCTCGGCTACGGCGCCTATGCA GCGGCCAACGCCTACATGGACAGCTTCGCCCGCCGCCACGATCGGCCGGACGAATGTCGTTGG GCGCGCCTGGCGATCGTGCCCGAGGACGCTCCGGCCCTGTTCGCGCGGGTGCTAGAGCGACTT $\verb|CCGCAATCGTTCATCGTGTCCACCGCCGACCTTCGGGCCCGCATCGACACTTGGATCCGGGAC| \\$ AAGAACCGCGTCCCGCCGGGGATCCGAGCGGTTCAACCGCGACCGGACCTGAGCCAGGCG TACGCCCGCCGATCGGCCCGCTGGAGATTCAACTCTGCGGGCTGGTCTCCGCCTATTGCCGG TTCGACCGGATCGGCCGGACGATTCCTTCTTCGAAATCGGCCTCAGCTCGTTCGACTTGATC CAGCTCAGCTCGCGCATTCACCGGCAAGGATCTCAATACGACCCAACTGTTCAGC TACCCCACCGTGCGCGCCTTTGGCGCTCTTCCTCGGCGGCGAACCGGAGGGGCTCGCGGCGGAG GAGCCCGCCATGGAGAACCTGTGGCTGCAACGAAGCGATGCGACCCTCGATGAG

(2) peptide sequence

Seq ID No 64 (>pEPOCOS6_ORF12.pep)

MTVEHETGFEIAVIGLACRVPGAADVAAFWRNLVEAKESVRFFEDHELRAAGVPEEILRLPNY
VKAKPLLADGEAFDADFFGFHPREAAYLDPQVRLLHECCWTALEDAGYDPAQYAYPIGLFAGV
SSNLSFLFDRIDPRDSPLQKRYVAELNAASFATQIAYRLDLKGPAISIQTACSTSLVAIHLAA
QSLIGGECHMALAGGATLEVPKKPGYLYREGYINSPDGHCRAFDADAAGTIFGDGVGIVLLKR
YRDALRDGDHVYAVIKGSAINSDGHRKVSYTAPGKSGQVAVIRAALAAAQVEPQTIRFVEAHG
TGTLAGDPIEVEALTEVFAEAGRGTCALGSVKTNIGHLDVAAGVAGFIKAVLALERRVLPPSL
HFVRPNPAIDFNGPFYVCRQIERLTENGRLRAGVSSFGIGGTNAHVILEEAPAPEARLPAGSP
PGASPFLFPLSAKTPDALAGRCHDLADHLRAHPELLLADVALTLQMGRASFAYRHVVQAATAE

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ELIRGLGAFRQESIRKRRNRVQWVLAGEAMSLDAGLRLYADWPVYRERVDVCLAIVAKLRQID GRSFLHEWIERPREVPAEWSTALAFMFHCALAQALSQAGLHPQRMWSRGLGGQVGVVLAESLS LEGALALVLCQTPVPGDATPQRERLVRTLEGCRFRPPRFLISADSSGRPLDLAEFAHVDFWCG GOSASPNEAELRSWSDAAPELVTLAIGPSFLEAASGTVGLAIDPKRPMTCVQRTVAALWEWGC DVRWAAFTSSTGRRVPLPTYPFVRVIPTIGDPLRGAGAEDDLIAASASASAGSPPEPSANSAA ERPRAQSSIASATTPAPSHTSASVAVATILETVRAYFGFAAVRSTDAFFELGASSLDLVNLGQ LLSDRLGREVPTLLLYDHPTPDQLALALTSAALSAEAPPLRGGHRASTSGTAASSAASTAPTF PGDAHSQPSFVREQDIAIIGMAFRGPGADDLDAFWNNLVEGVESITFFSEDELLAAGVPREHL ASTRYVRAKGELTGMMDFEPEFFGYSAREAAVMDPQFRVFHECSWHALEHGGYDPTRCAASIG VYAGVTNHLPWLMRTLPHLTEEEÇFGALLLTDREFFAPLLSYKVGLRGPAISLQTACSTSLVA IGTACRELRAGACQMALAGGVTAS I ERCGYFHQEGYILSPDGHTRSFDAAAAGTVFGDGVGMV LLKPLAQALADGDTIHAVIKGIGINNDGARKVGFTAPSRAGQTEAIRAALRDAGVASNRVSYV EAHGTATRMGDPIEVEALTQAFRAEADGPLPPGSCLLGSVKSNVGHLNAAAGVAGLVKTVLAL QHRRLPTSLFYQSPNPHIDFAASFFRVNGQTSDWVAPEGTRLLAGVSSFGIGGTNAHLIVEEA PKALPTTAAPLSTEPNDLDAGDACGLVLPISARTPTALAHIATNLANHLERHPTIALADVALT 15 LQLGRRQWPHRHSLICRNRTEAIKLLRAVVHSAEVPPAQAPVSDAPRCVFLFPGQGAQYPSMA $\verb"RDLVRNCPDFALHLDPCLDQLAELLPEDPRCILFGDGPADRLDQTAYTQPLLFSVSYALARWL"$ GDFGIRPDAMIGHSLGEYVAACLAGLFSLSDALLLVSERGRLMGSAARGAMLAVPLPEWELEE RLELLADDRISIAAVNTAESCVIAGPSEAIERCAQRWAAQGLTCTPLRTSHAFHSAMMEPIVE 20 PFGHVLARVTFAPPRARWISNLDGKPIDSAAVMQPDYWVRHLRQPVRFHEGLSHLLAEDTHAW VEVGPGRTLSSFVRRHPAYRHQPIVNPMRHAVESTGDVRRWRQALGELWRAGMPVAWERORRG RHAGRRVPLPGYPFERRPFAARRFVELAQPAPKAELVKNPDPARWLYRRVWRPAQAAAGGLAV QATVLVFGDGSELCRAAVAQVQRQGLKCVSITAGRQFARESDMRFTLDPADPRQLDQLFAALD GSGSRPRYVLHLLTLNPPPDASAIIAHSYYSPMALAHALGAHEIAPVSITVVTAGVVAVADEA 25 IREPLQALIVGPCLVIPQEFPGLSVRLLDVNVDDPAPRLAERLVAELSGTDHMVALRGGERLV ${ t ADVDQVDGLGVGIAKVPLRREGHYLILGGLGDIGYHCARYLAQTYRAKLTLTARSSLPPRASW}$ ERMLREGNLDSRQRTRIERVLSLEACGAEVQTAAVDLGDRHRLADVFREARGRFGAIAGVIHS AGT PGHVHSIDELVRVRDEAQFTAKVRGLHHLAEVVDPLNLDFCLLFSSLSTVLGGLGYGAYA AAMAYMDSFARRHDRPDECRWIAVNWDAWLFEAKTSSVGAELARLAIVPEDAPALFARVLERL PQSFIVSTADLRARIDTWIRDKNRVPPAEIRAVQPRPDLSQAYAPPIGPLEIQLCGLVSAYCR 30

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FDRIGRDDSFFEIGLSSFDLIQLSSRIHRITGKDLNTTQLFSYPTVRALALFLGGEPEGLAAE EPAMENLWLQRSDATLDE

pEPOcos6_ORF13 sequences:

(1) nucleotide sequence

Seq ID No 65 (>pEPOcos6_ORF13.seq)

TTCCGACTGTTGCCGCTTTCGGCCAAGACACCCGGCTGCGCTCGAAGCGAAGCGCCGCGATCTG
30 GCCGGCTTCCTCGAACGCCACCCGGAGACCTCCTTGGCCGACCTCGCTTTACCCTGCAACGC

GGCCGCGAGGTCTTCAGTCACCGCGCCTGCCTCGCCGTGGAGACCTTAACGTCCGCGCGCACG $\tt CGGCTGAGCGGCGAGTCGTCGAGCACTTGCGTGGTGGGCCCCGCGCCCAGCGCCATATTTCTG$ 10 TTCCCTGGTCAAGGCAGCCAGCTCGCCGGGATGGGCCGCGGTCTGTATCACCATTTCGAGCCG TTCCGCACGGCCGTCGATGCCTGTCTGCGCGAGCTGGAGCCAGGACTGCGGCAAGCGCTCAGC GCCCATTTCGATCCGAATCGCGGCGCGGACCCACCCGATTCGACGACCTTCGTCCAACCCTTG TTGTTCCTCGTCGAGTACGGGGTGACCGAGTGGCTACGCTGCTTGGGTGTGCGGCCAACAATG 15 GTGTTGGGTCACAGCTCTGGCGAGTATGCCGCAGCCTGCGTCGCGGGGCGTTCTGTCGCCGTCC CTCGGCGTCCCGCTGGCCGCGAGGCGCTCGAGGCGATGTTGCCCGACGCTCTCGATCTGGCG 20 10 GCGATCAACGGCTGTCAGCTTTGCGCCGTGTCCGGGCCGGTCGCGGCCGTCCACGCCTTCAAG GCCCAACTGGAAGCCGCCGGACATCACGCCCGCCTGTTGCACACCGATCGCGCCTTCCACTCG $\tt CCGCAAGTACCTTACCTCTCGACCGTCAGCGGGCGATTGGAGGCGGATGGGCCGGCGAACCCG$ 25 15 CCGGTGGATTCCTTCGTGTGCATCGAGGTGGGACCAGGCTCGGCCTTGAGCACCATGGCGCGC GAAACGTTGGGTTCCCAGGCGCGACTGATTTCGTTGCTGCCGCGGCCGCGAACGGGGCAAATC 30 GAGCCCGGTCCGGTATTCGAACGACTGGCGGCGCTTTGGCGCAGCGGGTTGACATTGGATTGG TCTAAATTGACGGCCGAAGAGGGTCATCGAATTCCCTTGCCAGTCTACCCGTTTCAGCGC AGCCATCTGTCGAGCTCCCTGGCGGCCGGCCACACGCCTTCGTCGCGGCCTGCAGTCGAATCA GGCGCCATCCTTGCCGAGCGATCCGCAGGGGAAAACGCTGAAACCCGGGATTGCCCGCTGCCA 35 ACCGCCACGCTCGAGCCCAAGGCGGTCGCTCCGGCCCCACTCGAGGCTACCGACGCCGCAGGT ACTCGCGAGCGACTGGCCGAACTTTGGCGCGAGTTGCTAGGGTTGACCTCGATTGGGCCCGAC GACCATTTCTTCGACCTGGGCGGCCACTCGCTGACCGCCACGCGGCTGCGCCCCTGATTCAC CAGCGGTTCGATGTCGGGCTCGGGCTCGACGAAATCTTCGCTCATTCGCGTCTCTCCCAGCTG 40 GCCGCCCGTATCGAGGCGGCCCAAGAGCCGATTTTCCTCCATTCCCAGCGCGCCGGACCAG GACGACTATCCCTTGTCATCCGCCCAGCAGCGGATTCACAGCATCGTCACGAGGGCCGAGGTC GGCACTGCTTATAATTTTCCGATCGTCCTCGAGCTGCAGGGCGCTCTGGATCGAGTGCGATTC 45 GAGGCGACGTTCGCGGCATTGTTCCGGCGTCATGAGGGGTTCCGCACCCGCTTTGTGATGCGC GATGGCGGGCCGCCAGCGCATTGTACCGGACGTGGCGTTTCGCCTGCCGCTCACCCAGGTC GAGCCAGAGCAGGTTCCCGGGCGCATCGAGGCCTTCATCCGTCCCTTCGATTTGGAACGCGCG

 $\tt CCGCTGTTCCGCGCGGAGCTGTTGCAGTTGGCCGAGCAGCGCCATCTGCTACTTTTCGACATG$ 10 GTCGCCACGCTGGCGCTCCCCGATTTCCCGCGTCCGGCGGTGCGCCGCTACAAGGGCCGT AATGTGGTGTTCCACCTGGACCGGAGATCCGCGACCGCCTGGTGGCCCTGGCTCGAACCCAG 15 GGGGTCACCATGAACGTGATGATGCTGGCGCTCTGGGCTGCTGCATCGCGAAACCGGC ${\tt ATCGGGCTCTTCACCAACTTTTTGCCCTTGCGGTTGGCGGTCGAGGGATCGACCCGCTTCGAT}$ 20 10 $\tt CGCTTCCTTGCCGCTTGCCACCAGGTGTTTCTCGAAGCCTATCAGCGCCAGGACTATCCGTTC$ CACTTGTTAGTCCAGGAACTCGTGCCGGTCAGGGACCCGTCGCGGTCGCCGCTGTTCCAGACC TCGCTCGTCTACCACAACGAAATTGACGGCAAGACCAAGCTGGAATTGGAAGGCTGAAAGTC GAAGTGGTTCCCTTCGAAAAGGGTGTGGCGAGGCTGGATTTGAAGCTGGATGTGACACCTTTT 25 15 GGCCTGATCGCGGGGTTCCAGGCGTTGGTGGCGGGGCTTGTCGCCGATCCGGCGCAATCGCTC GCCGCCGCGAGCGTTTCCGGGAAGCGGGCGCTGCCGCGGGGCGTGGCCACGGCAAGCGAATCG 30 TCGCCGCAGTCACTGCCGCCGCAACCATCGACGGCGTACGCCACTCCCTCACCGCAGTCACCG TCGCCGGTAGTCCTGACGGGACCCGCCGACCTGCCCGCGATCTTGGCGGCCTACGTGGGGCAG 35 GATCGCGCGCGCGCGTGGATAAGTTGGAATTGACCAGCCTGGTGCGGCTCGACGACCTGCGC GGGTTGGTCAATCCTCAGGCGAATGCCTTCACCCTGGCTTGGCGCGATCTGGCGATGCCGTTC ${\tt GGGGAGGGGCGTCCCCTGTGGCGACTCCGCCTGGCTGGTCGGCTCCATCGCGCTGGTTGCTA}$ TTGCTGACGGTTCATCCATTGATCGGCGACAACGGCACGGTCGACCTCTTTCTGGCGGCACTC 40 GCCGATCACCTGCGCCGCGCGCTCCGCTTTTCCCGTAGCACCGCTCGATGAGGCCGAGCTGGAG GCGGAGCTGAAGTGGGGAGAGGAAGGGGAGGGCCTCGGGCTGACCGCGATCGCGCCGGTCCTG ${\tt GGCCAATTGCGCGAAAGTCGGCTGAGTCCTGTGGCCCAGATGTGGCTGGACGAGGTCTGTCGC}$ 45 CGCCACGACCTCACCCCGCTAGAGGTCTTGGCGGCCCGGCTCCTCGATTGGACACGAAGCCAC GGTCACGGGTCGATCGCTTTGTGGACGCCGCTGCCCGAGGACCATCCGCTTCGCGATGAAGGC

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5 CGGGCGCGATCTGATGCGTTTCCTCGACGGCTTGGGCCCGGAAAGC

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(2) peptide sequence

Seq ID No 66 (>pEPOcos6 ORF13.pep)

MKYETTGLELAVIGLACRFPGSPDPEQFWSNLRAGRSGIRHFSDAELSHIPASLRHHPHYVKA KGALDHADFEPAFFGYSPKEAEVMDPQFRLLHECCWEALESGGYAPSQFAGRIGLFAAAAFND GWIAGTLDRLRTGVGLSSLETAFLTLRDYLTTQISYRLDLRGPSLLVQTACSSSLVAVQLAQQ ALISGECALALAGGVCATDPLHSGYLYEPGNIYARDGVCRPFDEAGAGTVFGDGCGMVLLKRL SDAQRDGDTIWAVIRGAGVNNDGHHKVGYTAPGTRGQVALLKSVYRASRVDPATLGYLEAHGT GTALGDPIEVEALTQAFASKRRGTCGLGSVKGNLGHLNTAAGIAGLIKVVLALKHREVPPTLN LRRPNPKIRFDETPFFPVVELQPWPSGTGPLRAGVSSFGIGGTNAHVILEEAPPTANPAPHGR FRLLPLSAKTPAALEAKRRDLAGFLERHPETSLADLAFTLQRGREVFSHRACLAVETLTSART RLSGESSSTCVVGPAPSAIFLFPGQGSQLAGMGRGLYHHFEPFRTAVDACLRELEPGLRQALS AHFDPNRGADPPDSTTFVQPLLFLVEYGVTEWLRCLGVRPTMVLGHSSGEYAAACVAGVLSPS AAVSLLAERERLLRDLPAGAMLGVPLAAEALEAMLPDALDLAAINGCQLCAVSGPVAAVHAFK AQLEAAGHHARLLHTDRAFHSRLVAFVLDRFQAAVQHVELRRPQVPYLSTVSGRLEADGPANP HYWVRHLRDTVRFGPALEALPPVDSFVCIEVGPGSALSTMARETLGSQARLISLLPRPRTGQI EPGPVFERLAALWRSGLTLDWSKLTGGEEGHRIPLPVYPFQRSHLSSSLAAGHTPSSRPAVES GAILAERSAGENAETRDCPLPTATLEPKAVAPAPLEATDAAGTRERLAELWRELLGLTSIGPD $\tt DHFFDLGGHSLTATRLRALIHQRFDVDLGLDEIFAHSRLSQLAARIEAAAKSRFSSIPSAPDQ$ DDYPLSSAQQRIHSIVTRAEVGTAYNFPIVLELQGALDRVRFEATFAALFRRHEGFRTRFVMR DGGPRQRIVPDVAFRLPLTQVEPEQVPGRIEAFIRPFDLERAPLFRAELLQLAEQRHLLLFDM HNLIADGISLNLFVADFAALYHGRPLAPLKLRYRDYAVWQEARLASDDLRSQREWWHRRLSPP

VATLALPPDFPRPAVRRYKGRNVVFHLDREIRDRLVALARTQGVTMNVMMLALWAALLHRETG QSELVVGSLLGGRPHSELHPVIGLFTNFLPLRLAVEGSTRFDRFLAACHQVFLEAYQRQDYPF

HLLVQELVPVRDPSRSPLFQTSLVYHNEIDGKTKLELEGLKVEVVPFEKGVARLDLKLDVTPF

PCT/US99/23535

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SDRLECVLQYDLDLFCEETMRGLIARFQALVAGLVADPAQSLAAASVSGKRALRAGVATASES

SPQSLPPQPSTAYATPSPQSPSPVVLTGPADLPAILAAYVGQNPHPFAIHRGLILEAPLGLRA
LRSALDAVLGEHTHWRSVRAGDRARRVDKLELTSLVRLDDLRGLVNPQANAFTLAWRDLAMPF
GEGRPLWRLRLAWSAPSRWLLLLTVHPLIGDNGTVDLFLAALADHLRRASAFPVAPLDEAELE
5 AELKWGEEGEGLGLTAIAPVLGQLRESRLSPVAQMWLDEVCRRHDLTPLEVLAARLLDWTRSH
GHGSIALWTPLPEDHPLRDEGRCLQVRLLEGPPSQRGAGDPSWLEQIALRRGTPATEVVCPTP
TQRAAIDLALAWLPQPPLHGLVGTVQPWPESPLVCPFPLNLAFRPSHPIAYALKHEATLAVTA
RARDLMRFLDGLGPES

10 pEPOcos6_ORF13.1 sequences:

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(1) nucleotide sequence

20 CTTCCGCCGCCGGGCGGCAGGTGCAGGATGGTCGGGCATGG

(2)peptide sequence

Seq ID No 68 (>pEPOcos6_ORF13.1.pep)
MTQASAASTSQVAPEVTPGRKDDDDDQIRDVGRCSLCGERLPRWATRGRRDEAGPDAGAGRRE

25 AAPRPGEAEVAAPGARPAPERAAYPGGVGRLPRERGMTRAPPAGATMTPPHGASRPARRRASG LPPPGGQVQDGRAW

pEPOcos6_ORF14 sequences:

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(1) nucleotide sequence

Seq ID No 69 (>pEPOcos6_ORF14.seq)

TTTTTCTTTCAATATCGTCCTCTTCATATACGAGGTGAGTTCTCTGAGGTCCTCCTATAAG
TCTGGGGTGTCCTATTCGGCCTCTTACTTGTTACTTCGCCTTCTTAGGAGTTTTTCCTTAATT

TTGCCCTCTTACATTCCCGTATTCATTCTAACTGGGCCCTATCTCATTCGC

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(2)peptide :	secuence
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Seq ID No 70 (>pEPOcos6_ORF14.pep)

MVTRPTSDGIEDELAPFPPVLRGWLIEGELGRGGMGRVFRARHPKTRARAAIKVLLGDYARRP
DVVARFRQEAIAVNIINHPGIVRVFDSGELEDGSPYIVMEYLDGRGLRDWVQAVPPAERPRQV
VRLGYQIASAMAAAHASKVVHRDLKPENIMVVEDELAPGGSRVKILDFGIAKVLWGGLPEVLE
LEGRGSLAPASASTIRTELSTRPAPTVGATTGPESPLGASATPESALGASATPESALGASATP
ESEAHEEDALRSLPVVTSGRPAIHPAPVEIPPEAVSSAASRGSRASIEPGAPAPQSEGAGQPT
MPFTQEGVWGLGTRSYMAPEQERHSGSVDVKADVYSLGVILYELLEGRTPDAPSAAWPPPMSA
ATPPDLVALVHRVLAFDPDARPRMAEVASALHRLGRAKKELDEALSRWVVGGGAPGLLPCGYA

LUELVLLGPGNLYDSFQPVSAFFFQYRPLFIYEVSSLRSSYKSGVSYSASYLLLRLLRSFSLI LPSYIPVFILTGPYLIR,

or DNA sequences complementary to said open reading frames,

- 15 (b) DNA-sequences which hybridise under stringent conditions to regions of DNA sequences according to (a) encoding proteins or to fragments of said DNA sequences,
- (c) DNA-sequences which hybridise to the DNA-sequences accord-20 ing to (a) and (b) because of a degeneration of the genetic code,
 - (d) allele variations and mutants resulting by substitution, insertion or deletion of nucleotides or inversion of nucleotide segments of DNA-sequences according to (a) to (c), wherein the variations and mutants offer isofunctional expression products.
- 10. DNA sequence according to any of claims 1 to 5, wherein the DNA is selected from the group consisting of

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(a) the following DNA Sequence:

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Seq ID No 71 (>Contig43)

CGGGTATTTGTGATATGTGGGCNGTAGTCGTATGCTTCATTAAGTACATC 5 CGTCCGTNGTAGAGAGTGACTCTGTCGCAGCGATAATAGACACGCTTGTG ATGCTATAGGGAACATAGAGTCNTAGTAGATGATACGACGAGATATTNGT ATAGAGCGTATAGACCGACGTGTGAGCGTCATAAGTGTTGTGTGTCATGA TCAATGCTGCAAGNTATTCGTCGAATCTACATTATATCGAATCGTGTATG TGCGTTTGTCGCAGCGCGATNCGATGAGATACCGAAAGGGTATGTATCTA 10 TNTTCGTGACGCTCGATNAGAGCAAATCCGCTACCGTGGAGATATCGTGT ATCGACTCCATCACGATCAGTATCATGATACGTCAAACGAGTACACTCAT TATTGATAACACACGTANGTGTGCATGCACAGTTATCGAGTGTATTGTGT GCATGAGAGGTATAGGATNTATAGGCGAGCATATATATCTATATATATAG 15 GTTAAGAGTAGAANACTATGAAGATGCAGGAAGTAGTATCTCGCGGACAA ACGGNGTACCTAGCGGGGTTGAAGTATTATCGACAGTGTATAACGACTCA ACAGGONTACGAGGTACATTGTATTTACAGTGGTTGGAAGGATTGCGCGA GGAAAGGTAGTGGTACCGTGTGAGCTACGATGCTCGGGATAATGGTGATT

AGATAGAACCTTAGCGTTGCTAGATGAGTGAGTGGTGGTATGAGTAGAGT

20 TTTTGTTCTAGCTTTGTGTCCAGCGAGGATTCGTTCAGTCTGAAGGGTAA
GAGTACGTCCATCGCACACCCGACCGTTTTGAGGAGTTCTCGGTGCGTGG
TCAGTGGGGTTTGGAGAAGACAGAGTTGATTCATAGGGTTATCAAACGAG
TTATGTGGATAGATGGTAGTGACCCCATTTGAGTGAGAGTGTTGGCGTTA

ACANCAGCAGGATNTAT

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SEQ ID No 72 (>Contig44)

TAGGTCTTTGACACCATGGGAGCTGCTACCGATGTTGCCGAGCACGATCG
CGCTGGCGCCGACGAGCGACTGCAAGCCGGCCGGCCATTTACGCCTGA
CGAGCGAGGGGGGGAAGTGCTGGTGCGCGCGTGCGTGCGAGCGCGCC
CAGGTCCGCCGTTGCGCCGTCGCCGAGCAGTAGCGCGCCGTCGAAGACGA

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ATGCCGAGCACGCCGGCCGCGCCGTAGACGAGCTTGGCGCCCATGCC 10 TCAACGCGCCGAAGCGCGAGGCGATCGCGCCCCTGCGCGATCAGCGCG 5 GCGCCGAATACGATCGTGGCGATCTGAGGTGAGCTCTACTGGCATGATCC 15 CCGTCAGCCCGAGGATGGTGAGGACAATCGTCGCGGCGCCGCACAGTACC TCGCACGAGCGAGCCTCCGAGCACGACCTTCGGCGTCGTCTCTTTG GTCTGCGTCGCGCGCCGAGTGCGGCGTTATGTGGCTCTCCGGCTGTGCA AACCGTTCACGTTCTTCCGGTCCTGGAGTCAGCATCGGCATGATTCCCCC 20 10 GTCCTGCGGTGAGGCCTTGTCGCGCTCACGCGCGCTCCGACTTGCACGTG CTGTGCCGGGTTCTCTCGCTCAGGAGGCGCCTCTCTTGGTGGTGCTTGCG TCCTGGTCCGTTTGCCCGCCTGTGCGGTAGGTTTCTTGAACCAGGTGACC TTCAGGGACCCCTTGATGCGCTCCATCGTGTCCTATGTCGATCCTTCTCT 25 GACTTGTATGGGTCTCGAACCAACTACGCTTGATCAGGCCTTCGAAGGGT CCTTTGGGAGATCGACTCTGGATCCATACCGGGAGCCCCTGTTCTGCCGC TCTCTTAAGTTTCCCCTTCTGTATCCGTGTCGACCGGAAACGCTTTATCT 30 CTAATGCGCTCTAATTGCGTCTCTGCCACACGTGCGCTTCACTCTGGATC TACTTCTTCTCCCTAGTCTTCTACCTCCGTACCCTTATTTGTTGGTTCTA ${\tt TTTATTTCTTTTCGCTTCACCTCGCGTCATTGTCGCCTAGTGTTCCTCCC}$ 20 35 CTTTCCGGCTCCTCTTCTGCTGGCCCCTTATCCTTTCTAATACTTC

SEQ ID No 73 (>Contig48)

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15 SEQ ID No 74 (>Contig49)

ACCACCGCTTCACTCAGTATGTACTTTGTTATACTCGTCTTAGTACAATG

ATATAATACTCATGTGTATTCTTAATCTCGGGGAGANAAAATTGGAATAC

TGGACACCGTTGCCGCATGCNGACTCTAGAGATCCCCCTGCGACGGTATC
CCACGGCACCGGTATGGCCGGCGCGCGCTCCGGGGGTCAACGCCCCGTGG
TTGCCTTCACGACAACGCCGGTCGGGCGCGCGCGCGCTTCGATGCCGCGGG

CCCACAGCAGCGGATAGACCTTGAGCCAGTAGTTGACGAAATAGTCGCGC

10		AGCGAGAACTCCGGGGCGGCGGCCTTCATCCGCAGCAGGCTCGCCGCATG
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		AGGTCCCCCCGTGCACCTGCGCGGCGAGCTGCGCGGGCAGCCCGCGGAG
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		CGCGGCGCGTACGGCCGCGAACGACGTCACGATGCCGGCGTAAAGGGC
		GAGGAAGCACGGGCTCGAGATGACCAGGCCCGAGGCGCTATAGAGGGTGC
20		GCGCGGCCTCGAACGGCGCGCCCGTGCTGTGGCTGGGGAGCAGCGGCAGC
	10	CCGAACACGAGCCATGTGACGACGCCCCGAACAGGCACGCTGCCAGACG
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25		CTTGCCGGTGCAGGCTCACGAAGGTCGGCACGAGGACGACGAAGATGACG
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30	15	CGCCTAAAACTAATGATCCGTTCTCAAATTGGTCAAAAAAAA
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35		TCTTATATATTCTCTTGTGATAATATATCGAGTGTGGGTACTCAGC
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		CACACTCTCCGGTCATATCTCGCATAATAGATATATTTTATATGTTCCG
		${\tt CGTTTTATCCGAGTGGGATACACTTTTTCTATATTTTCTTTGGTGTGACG}$
40		$\tt CGTGGCGTCGAGCCTTATTATTGATTTGGTAGTCACGATATTCTCTAGAT$
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	25	GACTCTCACTCTT
45		SEQ ID No 75 (>Contig50
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GCGGTGAGCTTCCTGGCGTTGCTCCTCGTCGTCGCCGACGTCGC GACGCGGAACACGTTCCCGCCCGCGCGCTTTGCCGGCGCTGAGCCCGCCGG 10 CGCCGGCGCTGATCCCGCCGGTGCCGGGCGGATCCGTTGGGCCGTCGCCG GAGCCGCTGTCGGTCGGCCGGTGATCGGTTGTGCGGGCGCCGTGCCTCGG GATGAAAATCGTGATCGCCACGTGCGCGTTGTTCTAGATCGTCCCAGGCT 15 GACCGTCGGGAGCGCCCAGCACGAGATGAAGAGCCACACCGCGAGGACCG TGTTGAGGTACCGCACCGCAGGGGGGGGAGCATGGCGGTGATCGCGAAGATC ATGCAGAGCAGCCCGAGCACCCATGTGTTCGTCCGCTGCGCGTGGCTGTG 20 CGGCCAGATGACGGCCGAGATGAGGAGCCAGAACCCGAGGACGACGTTCA 10 GATCATGGGACCGATCGGGTCGCCACGGATCGATAACGGGCGTCAGGAGA CCGTCAATCGGCGAGCTCGTGAGCCATGGCGACAGCCCGCCGACCGCGCC 25 GGCGGGTCTCTGGCCTGCTGGTCGCCGGCGGCGGCGATGGGCCTG 15 CCTCCGGTCGGGCCGCGCGCGCGCGCGCGCGCGAGCTGGAGAC TCTCGACGGCCGAGCGGCACTAAGCTTCCGTCATGAGGCTCGGCGCACG 30 GCTCACCACGCACACGTTCTCGGCCGGCGCCGGCATCAGCTTCGTCG TCCAGCCGATCCCGGGCTCGGACCAGCTGTTCGTCATTCCGATCCAGTAC CTGCTCGCGGCGTCGCTCGCGAAGGAGCGAGGCGCGCCGCTCTCGAAGGC 20 35 TCATGCTCGGCTTGACCCTAGGGCTGATCCCGCTGGCCGGCGCGTTCACG AACGCGATGACGGCGTTCCTCACGACCGAATATCTCGGGTACTACGTGGA TAGAGCCCTCGACAACCCGGACAATCCGCCTCCGGCCCTGTCGATCCAGG 40 ATGTCTTGGACGCCATCACCTCCTTCTTCACCGGGCGAGCGCGGTAGGCG 25 AGCGGTCCCTGGGTCGAGCCCACCCTGCGGCTCTAGGAGCCGAAGGGCGA GCTCCTCGGGAGCGGCGCGGCGTCACCACCAGATTCGCCGGCGCTTGCGG 45 CCGGAGCGTATCGCGACCGCCGCCACCGCCACGGCGAGCACGGTGAC CGCGGCGGCCGCGATGGCGACGCTCCGGGCCGTGTGCTCGGCCTCGC

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TCCCGGAGACCCGGTTGAGCACCTTGCGGCCCTGGTAGCGGCGTACGGCA GCGGTCGCCGCGCCCTTGTGGTCTGTTCCGAAAGGGCTGCCGCCCTCTC . 10 GGACTCTCCCGTTCCTCCCACGACTGCCACTTCCGCAAAGTCGCTGGTCA GTGGGGGGTGGGAAAACTCTGTCAACCCTTTACCTAGGCGTCCCTTTTTG CCAGGGGGGTCTCACGGGGGCCTCGGCGGCTCGGTCGGCGGCCTTCCG 15 GGCCCGCGCGCCCTTCTTGCACGCCTCGGAGCAGAACTCCTTGGCTC GCTTGCCGGGGGTGATCGTGAGGGCGCGCGCGCAGCGGCAACGGGGGCCG GCGGGGACGCGGGGGGGGGACTGAGTCGGCGCGCCGATCAAAGAGGGGGGT TGCGGACGCCAAAGCGTCCCTTACGCTGGACACAGACGAGTACCTTGGTT 20 10 GGTAGCCGGGTGGACGTCAGAAGCCGTCAGGGATTAGGACCCCTGGCCGT ACGCGTGGCTCGCCGCGGATGCCTCAGAGGCCCCACCGGTCGTCAGGA CGCAGACGTCGGCGTGCTCCTGGTGGTGAGTCACCAGCTCGACCACACGG 25 GCGCGGCCGGCGACGTCTC 15 SEQ ID No 77 (>Contig52) 30 CGGGATCTGGCCTTCATTAACCAACGACGGGGCAAACATAATAGGCTGGG CATTGCGCTTCAGCTCACCACAGCCCGTTTTCTGGGAACATTTCTGACGG ATTTAACTCAGGTTCTGCCTGGTGTTCAACATTTTGTCGCGGTACAGCTT AATATCCACCGTCCAGAAGTTCTCTCCCGCTATGCTGAACGGGACACTAC 20 35 CCTTAGAGAACATACTGCATTAATTAAGGAATATTACGGCTATCATGAAT TTGGTGATTTTCCATGGTCTTTCCGCCTGAAGCGTCTGCTATATACCCGG GCGTGGCTCAGTAATGAGCGACCGGGTCTGATGTTTGATTTTGCCACTGC ATGGTTGCTTCAAAATAAGGTATTACTGCCCGGAGCAACCACACTAGTAC 40 GTCTCATCAGTGAAATTCGTGAAAGGGCAAATCAGCGGCTGTGGAAAAAG 25 CTGGCCGCACTGCCGAACAAATGGCAGCAGCTCAAGTGATGGAGCTTCT GGTCATTCCGGAAGGTCAGCGTGTATCAGCACTGGAACAGTXXXXXXXX 45 ATCCGATTACGAAGTCTTGAGTTTTCCCGACTGAACTTTTCCGGTCTGCC TGCCATTCAACTGCGTAATCTGGCTCGTTATGCTGGCATGGCGTCGGTAA 30

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CTCTGGTCACGCGACTTCGTGCTGATATGATACCATCGTTCCATGTTACG CGAAGTTACTCATAAGATCTCCTCACACATCAACGAGTGTACTCCTATGT GTTTCATACAAACTCGATACCCTTCAGAGTAGTGTCATGCCTATGTGGTA TGCATAATGTTAGTATACTTT

SEQ ID No 79 (>Contig54)
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ACATGCGGATGGCGTGGGCTCGGCGAGGGCCTGGTCCACGATCCCCGCC GCGAGGCAGAGCCCGGATCCGAGCCGATCTGGCGCTTGTC CGGGCCGAGGCCCATCGCGAAGGTGCGCGCGTCGGGCATCCAGAAGGCGT CGTTGAACCGCCTCTGCAGCTCGAGCGCCTCGGCGAACAGCCGTCGCGCG TCGTCCTTGCGGCCGAACCAGAAGAGCAGCTCGGAGAGGCGCAGCTTCGA CAGGAACACGAAGCCCTGCATCTCGCACGTCCCGATCGGCGGCCGCACCT GAGAGCCGTCGGCGTGGACGATGGCGTCGTCGGAGTCCTTCCAGCCCTGG TTCTGGATCGACGCGCTCGAGCGGGGCTCGTACTCGTAGAACCCGTCGCC GTCGAGATCGCCCTCCTCGTCGATCCAGCGCATGGCCCTGAGCGCAGGCT CGATCAGGCGGCCGACGCGCTCGCGATCGCCGGTCCAGTGCCAGAGCTCC GAGGCGGCCACCGCGTAGAACATCGTCGAGGTCGCCGACGCGTACGTGCG CCCCAGCGGGTTGTAGTTGAGGTCCGAGAGCGCTCCGTCCCTGGCCTGAT GCAGCATCCGGTCGGGCTGCTCGTCGCGCCAGTCGTCGACGACGCCCCC CGCGGCGGCCTGCGTGCCCGCGGCGAGCGGGTCGCGGCCGAAGAGCCCGA TGTAGATCGGCAGTCCGGCGCCCACCGTCCAGGAGCGCTCGTCCTGGTCG ATATCGTACATGCGGAGCGCGATGAGATCGCGCTTGGCTCGAGCAC GGAGAAGACCGTATGCGAGAGCGTGTCGGCGCCCGGGACCGAGAAGGACG TGGCGCGGTGGTGGAAGGTGCCGCGCGCGCGCGCGCGTTTCGCGTG CCGAAGAACGAGCGGCAGCCGGCGAGCAGCGGAGCGGTTCGCCGCGGAT CAGGGCGATCACGTCGACGCAGCCGCCCAGGTGCCATGGGGCTCGAGAT CTCCGGGCCCGTACGACGATCCCGGCGTCGAAGCGCGCGGACGCCGGATTC TCCGGGGTGTTCATAGCGGTGCTCGGCGCGGTAGTCGCAGCGCAGCGCGC ATCCGTGCTCGGCGGGCTCGAGCGCCCACCGGGCGTCGCCGCGCTGGAGG CGCGGGCCGTCCGTCTCCGCGTCGGCGAAGTCGGCGTCGATCTCGAG CGCCAGCGTGAAGCGCACGCGCTCCTGCGTGAAGCTCGCGACGTCGATGT CCTCGTGGAAGCCGTCCCCCACGAAGCGCGACAGCCGCAGCTCGACGGTC CGCGGCGCCGCCGCCCTCGGGCGGGGGGGGGTGTAGTAGCCGAG

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30 ACAGTAAACTTTCTCTACGTAGATCGAGGAGAAGACTCAATTTGTTGACA

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CGCAACAGCGGCGAGGAGCAGGACGCATACGACATCACCGGCAATACG 10 CTCAGCGTCGCCGACGGACGGTTGTCTTATACGCTAGGGCTGCAGGGACC CTGCCTGACCGTCGACACGGTCTGCTCGTCGTCGTCGCCATCCACC TTGCCTGCCGCAGCCTGCGCGCTCGCGAGAGCGATCTCGCGCTGGCGGGA 15 GGCGTCAACATGCTCCTTTCGTCCAAGACGATGATAATGCTGGGGCGCAT CCAGGCGCTGTCGCCCGATGGCCACTGCCGGACATTCGACGCCTCGGCCA ACGGGTTCGTCCGTGGGGAGGCTGCGGTATGGTCGTGCTCAAACGGCTC TCCGACGCCCAGCGACACGCCGATCGGGTCTGGGCTCTGATCCGGGGTTC 20 10 GGCCATGAATCAGGATGGCCGGTCGACAGGGTTGATGGCACCCAATGTGC TCGCTCAGGAGGCGCTCTTGCGCGAGGCGCTGCAGAGCGCTCGCGTCGAC CGACCCGATCGAGGTCGAGGCGCTGCGTGTTGGGGCCGGCGCGCG 25 CCGATGGGAGCCGCTGCGTGCTGGGCGCAGTGAAGACAAACCTCGGCCAC 15 CTGGAGGCGCTGCAGGCGTGGCGGTTTGATCAAGGCGGCGCTGGCTCT GCACCACGAACTGATCCCGCGAAACCTCCATTTCCACACGCTCAATCCGC 30 GGATCCGGATCGAGGGGACCGCGCTCGCGCTGGCGACGGAGCCGGTGCCG TGGCCGCGGCCGGCCGCCTTCGCGGGGTGAGCGCGTTCGGCCT CAGCGGCACCAACGTCCATGTCGTGCTGGAGGAGGCGCCGGCCACGGTGC 20 TCGCACCGGCGACGCCGGGGCGCTCAGCGGAGCTTTTGGTGCTGTCGGCG 35 AAGAGCGCCGCCGCCGCGCACACAGGCGCGCGCGCTCTCAGCGCACAT CGCCGCGTACCCGGAGCAGGGTCTCGGAGACGTCGCGTTCAGCCTGGTAT CGACGCGTAGCCCGATGGAGCACCGGCTCGCGGTGGCGGCGACCTCGCGC GAGGCGCTGCGAAGCGCGCTGGAGGTTGCGGCGCAGGGGCAGACCCCGGC 40 25 AGGCGCGCGCGCAGGCCGCTTCCTCGCCCGGCAAGCTCGCCTTCC TGTTCGCCGGGCAGGCGCGCAGGTGCCGGGCATGGGCCGTGGGTTGTGG GAGGCGTGGCCGGCGTTCCGCGAGACCTTCGACCGGTGCGTCACGCTCTT 45 CGACCGGGAGCTCCATCAGCCGCTCTGCGAGGTGATGTGGGCCGAGCCGG GCAGCAGCAGGTCGTTGCTGGACCAGACGGCGTTCACCCAGCCGGCG CTCTTTGCGCTGGAGTACGCGCTGGCCGCGCTCTTCCGGTCGTGGGGCGT

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GGAGCCGGAGCTCGTCGCCGAGCTGGCCGCCT GCGTGGCGGTGTGTTCTCCCTCGAGGACGCCGTGCGCTTGGTGGTCGCG TGGTGTCGATCGCGGCAGTCAATGGGCCGGAGCAGGTGGTGATCGCGGGC GCCGAGAAATTCGTGCAGCAGATCGCGGCGGCGCGTTCGCGGCGCGGGGGGC GCGAACCAAACCGCTGCATGTCTCGCACGCGTTCCACTCGCCGCTCATGG ATCCGATGCTGGAGGCGTTCCGGCGGGTGACTGAGTCGGTGACGTACCGG CGGCCTTCGATCGCGCTGGTGAGCAACCTGAGCGGGAAGCCCTGCACCGA 10 TGAGGTGAGCGCGCGGGTTACTGGGTGCGTCACGCGCGAGAGGCGGTGC GCTTCGCGGACGGAGTGAAGGCGCTGCACGCGGCCGGTGCGGGCCTCTTC GCCGGATGCCAGGCCGGTGCTCCCAGCGTCGCGCGCGGGCGTGACG AGGCTGCGAGCGCGCTAGAGGCGCTGGGTGGGTTCTGGGTCGTCGGTGGA TCGGTCACCTGGTCGGGTGTCTTCCCTTCGGGCGGACGGCGGGTACCGCT GCCAACCTATCCCTGGCAGCGCGAGCGTTACTGGATCGAAGCGCCGGTCG ATCGTGAGGCGGACGGCACCGGCCGTGCTCGGGCGGGGGGCCACCCCCTT CTGGGTGAAGTCTTTTCCGTGTCGACCCATGCCGGTCTGCGCCTGTGGGA GACGACGCTGGACCGAAAGCGGCTGCCGTGGCTCGGCGAGCACCGGGCGC AGGGGGAGGTCGTGTTCCTGGCGCCGGGTACCTGGAGATGGCGCTGTCG 20 TCGGGGGCCGAGATCTTGGGCGATGGACCGATCCAGGTCACGGATGTGGT GCTCATCGAGACGCTGACCTTCGCGGGGGGATACGGCGGTACCGGTCCAGG TGGTGACGACCGAGGAGCGACCGGGACGGCTGCGGTTCCAGGTAGCGAGT 25 GCTGCGCCGGATCGGGCGCGTCGAGACCCCGGCGAGGTCGAACCTCGCCG ${\tt GCGCTCGCCGAGATGGGGGCTTCAATACGGCCCGGCGTTGCGGGGGCTCGC}$ AGGCCGCCGGCTCCGCGACAGCCTACCAGCTGCATCCGGTGCTGCTGGAC GCGTGCGTCCAAATGATTGTTGGCGCGTTCGCCGATCGCGATGAGGCGAC

GCCGTGGGCCCGGTGGAGGTGGGCTCGGTGCGGCTGTTCCAGCGGTCTC CTGGGGAGCTATGGTGCCATGCGCGCGTCGTGAGCGATGGTCAACAGGCC 10 TCCAGCCGGTGGAGCGCCGACTTTGAGTTGATGGACGGTACGGCCGCGGT GGTCGCCGAGATCTCCCGGCTGGTGGTGGAGCGGCTTGCGAGCGGTGTAC GCCGGCGCGACGACGACTGGTTCCTGGAGCTGGATTGGGAGCCCGCG 15 GCGCTCGGTGGCCCAAGATCACAGCCGGCCGGTGGCTGCTGCTCGGCGA GGGTGGTGGGCTCGGCGCTCGTTGTGCTCGGCGCTGAAGGCCGCCGGCC ATGTCGTCGTCCACGCCGCGGGGGACGACGAGCACTGCAGGAATGCGC GCGCTCCTGGCCAACGCGTTCGACGGCCAGGCCCCGACGGCCGTGGTGCA 20 10 CCTCAGCAGCCTCGACGGGGGGGGCGGGCCCGGGGCTCGGGGCGCGC AGGGCGCCCCGAGCCCCGGAGCCCAGATGTCGATGCCGATGCCCTC GAATCGGCGCTGATGCGTGGTTGCGACAGCGTGCTCTCCCTGGTGCAAGC GCTGGTCGGCATGGACCTCCGAAACGCGCCGCGGCTGTGGCTCTTGACCC 25 GCGGGGCTCAGGCGGCCGCCGCCGGCGATGTCTCCGTGGTGCAAGCGCCG CTGTTGGGGCTGGGCCGCACCATCGCCTTGGAGCACGCCGAGCTGCGCTG 15 TATCAGCGTCGACCTCGATCCAGCCGAGCCTGAAGGGGAAGCCGATGCTT 30 TGCTGGCCGAGCTACTTGCAGATGATGCCGAGGAGGAGGTCGCGCTGCGC GGTGGCGACCGGCTCGTTGCGCGGCTCGTCCACCGGCTGCCCGACGCTCA GCGCCGGGAGAAGGTCGAGCCCGCCGGTGACAGGCCGTTCCGGCTAGAGA TCGATGAACCCGGCGCGCTGGACCAACTGGTGCTCCGAGCCACGGGGCGG 20 35 CGCGCTCCTGGTCCGGGGGGGGGTCGAGATCTCCGTCGAAGCGGCGGGGCT CGACTCCATCGACATCCAGCTGGCGTTGGGCGTTGCTCCCAATGATCTGC CTGGAGAAGAAATCGAGCCGTTGGTGCTCGGAAGCGAGTGCGCCGGGCGC ATCGTCGCTGTGGGCGAGGGCGTGAACGGCCTTGTGGTGGGCCAGCCGGT 40 GATCGCCCTTGCGGCGGGGGTATTTGCTACCCATGTCACCACGTCGGCCA 25 CGCTGGTGTTGCCTCGGCCTCTGGGGGCTCTCGGCGACCGAGGCGGCCGCG ATGCCCTCGCGTATTTGACGGCCTGGTACGCCCTCGACAAGGTCGCCCA 45 GTCTTTGCGCGGTGCGATGGGCGCAGCGCGTGGGCGCCGAGGTGTATGCG ACCGCCGACACGCCCGAGAACCGTGCCTACCTGGAGTCGCTGGGCGTGCG 30

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GGACGGACGCGAGGGTGTGGACGTCGTGCTCGACTCGCTTTCGGGCGAG . 10 CGCATCGACAAGAGCCTCATGGTCCTGCGCGCCTGTGGTCGCCTTGTGAA GCTGGGCAGGCGACGACTGCGCCGACACGCAGCCTGGGCTGCCGCCGC TCCTACGGAATTTTTCCTTCTCGCAGGTGGACTTGCGGGGAATGATGCTC 15 GATCAACCGGCGAGGATCCGTGCGCTCCTCGACGAGCTGTTCGGGTTGGT CGCAGCCGGTGCCATCAGCCCACTGGGGTCGGGGTTGCGCGTTGGCGGAT CCCTCACGCCACCGGTCGAGACCTTCCCGATCTCTCGCGCAGCCGAG GCATTCCGGAGGATGGCGCAAGGACAGCATCTCGGGAAGCTCGTGCTCAC 20 ${\tt GCTGGACGACCCGGAGGTGCGGATCCGCGCTCGGCCGAATCCAGCGTCG}$ 10 CCGTCCGCGCGCACCTACCTTGTGACCGGCGGTCTGGGTGGCCTC GGTCTGCGCGTGGCCGGATGGCTGGCCGAGCGGGGCGCGGGGCAACTGGT GCTGGTGGGCCGCTCCGGTGCGGCGAGCGCAGCCAGCCGCCGTGG 25 CGGCGCTGGAGGCCCACGGCGCGCGCGTCACGGTGGCGAAAGCGGACGTC 15 GCCGATCGGTCACAGATCGAGCGGGTCCTCCGCGAGGTTACCGCGTCGGG GATGCCGCTGCGGGTGTCGTGCATGCGGCAGGTCTCGTGGATGACGGGC 30 TGCTGATGCAGCAGACTCCGGCGCGGGTTCCGCACGGTGATGGGACCTAAG GTCCAGGGGGCCTTGCACTTGCACACGCTGACACGCGAAGCGCCTCTTTC CTTCTTCGTGCTGTACGCTTCTGCAGCTGGGCTTTTCGGCTCGCCAGGCC 20 AGGGCAACTATGCCGCAGCCAACGCGTTCCTCGACGCCCTTTCGCATCAC 35 CGAAGGGCGCAGGGCCTGCCGGCGCTGAGCATCGACTGGGGCATGTTCAC GGAGGTGGGGATGGCCGTTGCGCAAGAAACCGTGGCGCGCGGCAGATCT CTCGCGGGATGCGGGGCATCACCCCCGATGAGGGTCTGTCAGCTCTGGCG CGCTTGCTCGAGGGTGATCGCGTGCAGACGGGGGTGATACCGATCACTCC 40 25 GCGGCAGTGGGTGGAGTTCTACCCGGCAACAGCGGCCTCACGGAGGTTGT CGCGGCTGGTGACCACGCAGCGCGCGGGGTCGCTGATCGGACCGCCGGGGAT 45 GCTGCTGCAGGACGTCGTGCGCGTGCAGGTCTCGCATGTGCTGCGTCTCC ${\tt CTGAAGACAAGATCGAGGTGGATGCCCCGCTCTCGAGCATGGGCATGGAC}$ TCGCTGATGAGCCTGGAGCTGCGCAACCGCATCGAGGCTGCGCTGGGCGT

CGCCGCGCCTGCAGCCTTGGGGTGGACGTACCCAACGGTAGCAGCGATAA CGCGCTGGCTCGACGACGCCCTCGTCGTCCGGCTTGGCGGCGGGTCG 10 GACACGGACGAATCGACGGCGAGCGCCGGTTCGTTCGTCCACGTCCTCCG CTTTCGTCCTGTCAAGCCGCGGGCTCGTCTCTTCTGTTTTCACGGTT CTGGCGGCTCGCCCGAGGGCTTCCGTTCCTGGTCGGAGAAGTCTGAGTGG AGCGATCTGGAAATCGTGGCCATGTGGCACGATCGCAGCCTCGCCTCCGA 15 GGACGCGCCTGGTAAGAAGTACGTCCAAGAGGCGGCCTCGCTGATTCAGC ACTATGCAGACGCACCGTTTGCGTTAGTAGGGTTCAGCCTGGGTGTCCGG TTCGTCATGGGGACAGCCGTGGAGCTCGCCAGTCGTTCCGGCGCACCGGC 20 TCCGCTGGCCGTCTTCACGTTGGGCGGCAGCTTGATCTCTTCAGAGA 10 TCACCCCGGAGATGGAGACCGATATAATAGCCAAGCTCTTCTTCCGAAAT GCCGCGGGTTTCGTGCGATCCACCCAACAAGTCCAGGCCGATGCTCGCGC AGACAAGGTCATCACAGACACCATGGTGGCTCCGGCCCCCGGGGACTCGA 25 AGGAGCCGCCGTGAAGATCGCGGTCCCTATCGTCGCCATCGCCGGCTCG 15 GACGATGTGATCGTGCCTCCGAGCGACGTTCAGGATCTACAATCTCGCAC CACGGAGCGCTTCTATATGCATCTCCTTCCCGGAGATCACGAATTTCTCG TCGATCGAGGGCGCGAGATCATGCACATCGTCGACTCGCATCTCAATCCG 30 CTGCTCGCCGCGAGGACGACGTCGTCAGGCCCCGCGTTCGAGGCAAAATG ATGGCAGCCTCCCTCGGGCGCGCGAGATGGTTGGGAGCAGCGTGGGCGCT 20 GGCGGCCGGCAGGCCGCAGGCGCATGAGCCTTCCTGGACGTTTGC 35 AGTATAGGAGATTTTATGACACAGGAGCAAGCGAATCAGAGTGAGACGAA GCCTGCTTTCGACTTCAAGCCGTTCGCGCCTGGGTACGCGGAGGACCCGT TCCCCGCGATCGAGCGCCTGAGAGAGGCAACCCCCATCTTCTACTGGGAT GAAGGCCGCTCCTGGGTCCTCACCCGATACCACGACGTGTCGGCGGTGTT 40 AGTACTCGTCGGCCATTCCCGAGCTCAGCGATATGAAGAAGTACGGATTG TTCGGGCTGCCGCAGGATCACGCTCGGGTCCGCAAGCTCGTCAACCC 45 GTCGTTTACGTCACGCGCCATCGACCTGCTGCGCGCCGAAATACAGCGCA CCGTCGACCAGCTGCTCGATGCTCCGCTCCGGACAAGAGGAGTTCGACGTT 30 GTGCGGGATTACGCGGAGGGAATCCCGATGCGCGCGATCAGCGCTCTGTT

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GAAGGTTCCGGCCGAGTGTGACGAGAAGTTCCGTCGCTTCGGCTCGGCGA CTGCGCGCGCGCGCGTGGGTTTGGTGCCCCAGGTCGATGAGGAGACC 10 AAGACCCTGCTCGCGTCACCGAGGGGCTCGCGCTGCTCCATGACGT CCTCGATGAGCGCGCAGGAACCCGCTCGAAAATGACGTCTTGACGATGC TGCTTCAGGCCGAGGCCGACGGCAGCAGCAGCACGAAGGAGCTGGTC GCGCTCGTGGGTGCGATTATCGCTGCTGGCACCGATACCACGATCTACCT 15 TATCGCGTTCGCTGTGCTCAACCTGCTGCGGTCGCCCGAGGCGCTCGAGC TGGTGAAGGCCGAGCCCGGGCTCATGAGGAACGCGCTCGATGAGGTGCTC 20 10 CCTGGAGTACTGCGGGGCATCGATCAAGAAAGGGGAGATGGTCTTTCTCC TGATCCCGAGCGCCCTGAGAGATGGGACTGTATTCTCCAGGCCAGACGTG TTTGATGTGCGACGGGACACGGGCGCGGGGCCCCCGCGTACGGTAGAGGCCC CCATGTCTGCCCCGGGGTGTCCCTTGCTCGCCTCGAGGCGGAGATCGCCG 25 15 GTGTTTGGATACCACCCCGCGTTCCGGAACATCGAATCACTCAACGTCAT CTTGAAGCCCTCCAAAGCTGGATAGCTCGCGGGGGTATCGCTTCCCGAAC 30 CTCATTCCCTCATGATACAGCTCGCGCGCGGGTGCTGTCTGCCGCGGGTG CGATTCGATCCAGCGGACAAGCCCATTGTCAGCGCGCGAAGATCGAATCC ACGGCCCGGAGAAGAGCCCGTCCGGGTGACGTCGGAAGAAGTGCCGGGCG CCGCCCTGGGAGCGCAAAGCTCGCTCGTTCGCGCTCAGCACGCCGCTCGT 20 35 CATGTCCGGCCCTGCACCCGCGCCGAGGAGCCGCCCCGCCCTGATGCACGG CCTCACCGAGCGCAGGTTCTGCTCTCGCTCGCTCGCCCTCGCGCTCGTCC TCCTGACCGCGCGCCTTCGGCGAGCTCGCGCGGCGGCTGCGCCAGCCC 40 25 CGGCGCGCTCGCTCCTGGGTTCCATCGAGTCCTCTTCCAGGATCCGGCGG TCGGGGTCGTCTCCGGCATCTCCTGGATAGGCGCGCTCGTCCTGCTG CTCATGGCGGGTATCGAGGTCGATGTGAGCATCCTGCGCAAGGAGGCGCG 45 CGGGGCCGCTGCAGCGCATGCAGGGCGCGTTCACGTGGGATCTCGAC GTCTCGCCGCGACGCTCTGCGCAAGCCTGAGCCTCGGCGCCTGCTCGTAC 30

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ACCTCGCCGGTGCTCGCCCCGCGGGACATCCGGCCGCCGCCGCGGGC CCAGCTCGAGCCGGACTGCCGGATGACGAGGCCGACGAGGCCGACGAGG 10 CGCTCCGCCCGTTCCGCGACGCGATCGCCGCGTACTCGGAGGCCGTTCGG TGGGCGGAGGCGCGCGGCCGGCTGGAGAGCCTCGTGCGGCTCGC GATCGTGCGGCTGGGCAAGGCGCTCGACAAGGTCCCTTTCGCGCACACGA 15 CGGCCGGCGTCTCCCAGATCGCCGGCAGACTCCAGAACGATGCGGTCTGG TTCGATGTCGCCGCGGGTACGCGAGCTTCCGCGCGGCGACGGAGCACGC GCTCCGCGACGCGGCCGTCGGCCATGGAGGCGCTCGCGGCCCGTACC GCGGATCGAGCCGCGTGTCCGCTGCCGTAGGGGAGTTTCGGGGGGAGGCG 20 GCGCGCCTTCACCCGCGGACCGTGTACCCGCGTCCGACCAGCAGATCCT 10 GACCGCGCTGCGCGCAGCCGAGCGGGCGCTCATCGCGCTCTACACTGCGT TCGCCCGTGAGGAGTGAGCCTCTCTCGGGCGCAGCCGAGCGGCGCGTGC CGGTGGTTCCCTCTTCGCAACCATGACCGGAGCCGCGCTCGGTCCGCGCA 25 GCGGCTAGCGCGCGCGGCAGAGATCGCTGGAGCGACAGGCGACGACC 15 CGCCCGAGGGTGTCGAACGGATTGCCGCAGCCCTCATTGCGGATCCCCTC CAGACACTCGTTCAGCTGCTTGGCGTCGATGCCGCCTGGGCACTCGCCGA 30 AGGTCAGCTCGCGCCACTCGGATCGGATCTTGTTCGAGCACGCGTCC TTGCTCGAATACTCCCGGTCTTGTCCGATGTTGTTGCACCGCGCCTCGCG GTCGCACCGCCCCCCCCACGATGCTATCGACGGCGCTGCCGACTGGCACCG GCGCCTCGCCCTGCGCCCACCCGGGGTTTGCGCCTCCCCGCCTGACCGC 35 TTTTCGCCGCCGCACGCCGCGAGCAGCTCATTCCCGACACCGAGATCAG GACACGTCACATCAGAGACTCTCCGCTCGGCTCGTCGGTTCGACAGCCGG CGACGGCCACGAGCAGAACCGTCCCCGACCAGAACAGCCGCATGCGGGTT 40 25 TCTCGCAACATGCCCCGACATCCTTGCGACTAGCGTGCCTCCGCTCGTGC CGAGATCGGCTGTCCTGTGCGACGGCAATATCCTGCGATCGGCCGGGCAG GAGGTACCGACACGGGCGCGGGGGGGGGGGGGGCCCACGGGCTCGAAAT 45 GTGCTGCGGCAGCCGCCTCCATGCCCGCAGCCGGGAACGCGGCGCCCGGC CAGCCTCGGGGTGACGCCGCAAACGGGAGATGCTCCCGGAGAGGCGCCGG GCACAGCCGAGCGCCGTCACCACCGTGCGCACTCGTGAGCTCCAGCTCCT

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CGGCATAGAAGACCGTCACTCCCGGTCCGTGTAGGCCATCGTGCTGAT CAGCGCGTTCTCCGCCTGACGCGAGTCGAGCCGGGTATGCTGCACGACAA 10 TGGGAACGTCCGATTCGATCACGCTGGCATAGTCCGTATCGCGCGGGATC GGCTCGGGTTCGGTCAGATCGTTGAACCGGACGTGCCGGGTGCGCCTCGC TGGGACGGTCACCCGGTACGGCCCGGCGGGGTCGCTGAAGTAGA 15 GTCTCATGGCTCGTCATCTGCGGCTCGGGTCCGTTGCTCCGGCCTGGGAT GTAGCCCTCTGCGATTGCCCAGCGCGCTCCGCCCGATCGGCTTCTCCATAT 20 GACGGCCTCTTCTCCCGACGCGCTCGGGGATCCATGGCTGAGGATCCTCG 10 CCGAGCGCTCCTTGCCGACCGGCGCGCCGAGCGCCCGACGGGCTTTGAAAG CACGCGACCGGACACGTGATGCCGGCGCGCGACGAGGCCGCCCCGCGTCTGA 25 AGCGTTGCGCGGTCATGGTCGTCCTCGCGTCACCGCCACCCGCCGATTCA 15 CATCCCACCGCGGCACGACGCTTGCTCAAACCGCGGGCGAGACGGCCGGGC GGCTGTGGTACCGGCCAGCCCGGACGCGAGGGCCCGAGAGGGACAGTGGGT 30 CCGCCGTGAAGCAGTGAGGCGATCGAGGTGGCAGATGAAACACGTTGACA CGGGCCGACGAGTCGGCCGCCGGATAGGGCTCACGCTCGGTCTCCTCGCG AGCATGGCGCTCGCCGGCTGTGGCGGCCCGAGCGAGAAAATCGTGCAGGG 20 CACGCGGCTCGCCCCGGCGCCGATGCGCACGTCGCCGACGTCGACC 35 CCGACGCCGCGCCGCCGGCTGGCGTCGTCACCTCTCGCCG CCCGAGCGCATCGAGGCCGGCAGCGAGCGGTTCGTCGTCTGGCAGCGTCC GAGCTCCGAGTCCCCGTGGCAACGGGTCGGAGTGCTCGACTACAACGCTG CCAGCCGAAGAGGCAAGCTGGCCGAGACGACCGTGCCGCATGCCAACTTC 40 25 GAGCTGCTCATCACCGTCGAGAAGCAGAGCAGCCCTCAGTCTCCATCTTC TGCCGCCGTCATCGGGCCGACGTCCGTCGGGTAACATCGCGCTATCAGCA GCGCTGAGCCCGCCAGCAGCCCCCAGAGCCCTCGCTCGATCGCCTTCTCC 45 ATCATATCATCCCTGCGTACTCCTCCAGCGACGGCCGCGTCGAAGCAACC GCCGTGCCGGCGCGCTCTACGTGCGCGACAGGAGAGCGTCCTGGCGCGG

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CGCGATCTACGGCGCCATCGCAGCCAACGTGGCGATCGCGGCGGTCAAGT TCATCGCCGCCGTGACCGGCAGCTCGGCGATGCTCTCCGAGGGCGTG . 10 CACTCCCTCGTCGATACTGCAGACGGGCTCCTCCTCCTGCTCGGCAAGCA CCGGAGCGCACGCCCGACGCCGAGCATCCGTTCGGCCACGGCAAGG AGCTCTATTTCTGGACGCTGATCGTCGCCATCATGATCTTCGCCGCGGGC 15 GGCGGCGTCTCGATCTACGAAGGGATCTTGCACCTCTTGCACCCGCGCCA GATCGAGGATCCGACGTGGAACTACGTCGTCCTCGGCGCGCGGCCGTCT TCGAGGGGACGTCGCTCATCATCTCGATCCACGAGTTCAAGAAGAAGGAC GGACAGGGCTACCTCGCGGCGATGCGGTCCAGCAAGGACCCGACGACGTT 20 10 CACGATCGTCCTGGAGGACTCCGCGGGCGCTCGCCGGGCTCACCATCGCCT TCCTCGGCGTCTGGCTCGGGCACCGCCTGGGAAACCCCTACCTCGACGGC GCGGCGTCGATCGGCATCGGCCTCGTGCTCGCCGGGTCGCGGTCTTCCT CGCCAGCCAGAGCCGTGGGCTCCTCGTGGGGGAGAGCGCGGACAGGGAGC 25 TCCTCGCCGCGATCCGCGCGCTCGCCAGCGCAGATCCTGGCGTGTCGGCG GTGGGGCCCCTGACGATGCACTTCGGTCCGCACGAAGTCCTGGTCGT GCTGCGCATCGAGTTCGACGCCGCGCTCACGGCGTCCGGGGTCGCGGAGG 30 CGAGGGAGCGCATCGAGACCCGGATACGGAGCGAGCGACCCGACGTGAAG CACATCTACGTCGAGGCCAGGTCGCTCCACCAGCGCGCGAGGGCGTGACG CGCCGTGGAGAGACCGCGCGCGCGCCCCCGCCATCCTCCGCGGCGCCCCGGG 20 35 GTCGTCCTTCGACGCGAGGTACGCTGGTTGCAAGTCGTCACGCCGTATCG CGAGGTCCGGCAGCCCGGAGCCCGGGCGGCGCGCACGAAGGCGCG GCGAGCGCAGGCTTCGAGGGGGGGCGCACGTCATGAGGAAGGCCAGGGCGCA TGGGGCGATGCTCGGCGGCGAGATGACGGCTGGCGTCGCGGCCTCCCCG 40 GCGCCGGCGCTTCGCGCGCGCTCCAGCGCGGTCGCTCGCGCGATCTC 25 GCCCGGCGCCGCTCATCGCCTCCGTGTCCCTCGCCGGCGCGCCCAGCAT GGCGGTCGTCTCGCTGTTCCAGCTCGGGATCATCGAGCGCCTGCCCGATC 45 CTCCGCTTCCAGGGTTCGATTCGGGCCAAGGTGACGAGCTCCGATATCGCG TTCGGGCTCACGATGCCGGACGCGCCCGCTCGCGCTCACCAGCTTCGCGTC CAACCTCGCGCTGGCTGGGGGGGGGGCGCCGAGCGCCCAGGAACACCC

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CCTGGATCCCCGTCGCCGTGGCGGCCGAGGCGGCCGTCGAGGCGGCCGTG TCCGGATGGCTCCTCGTCCAGATGCGACGGCGGGAGAGGGCCTGGTGCGC 10 GTACTGCCTGGTCGCCATGGCCGCCCAACATGGCCGTGTTCGCGCTCTCGC TCCCGGAAGGGTGGGCGCGCTGGGGAAGGCGCGAGCGCGCTCGTGACAG GACGGGCGGGCAGCCCGGCCATCGGAGGCCGGCGTGCACCCGCTCCG TCACGCCCCAGCCCGCGCGCGCGGGTGATCTCCCGCGGACAGGGCGCGTACCG 15 GCGACCCGCGCAACTCCGGCCCGCCGGGCATCGACATCTCCCGTGAG CAAGGGCACTCCGCTCCTGCCCGCGTCCGCGAACGATGGCTGCTTTT 20 10 CCACCCTGGAGCAACTCCGTTTACCGCGTGGCGCTCGTCGC CTCGGCGGGCGCCATCCTCGCGCTCATGATCTACGTCCGCACGCCGT GGAAGCGATACCAGTTCGAGCCCGTCGATCAGCCGGTGCAGTTCGATCAC CGCCATCACGTGCAGGACGACGCCATCGATTGCGTCTACTGCCACACCAC 25 GGTGACCCGCTCGCCCACGGCGGGGGGTGCCGCCGACGGCCACGTGCATGG 15 GGTGCCACAGCCAGATCTGGAATCAGAGCGTCATGCTCGAGCCCGTGCGG CGGAGCTGGTTCTCCGGCCACGCCGATCCCGTGGAACCGGGTGAAACTCC 30 GTGCCCGACTTCGTCTATTTCAACCACGCGATCCACGTGAACAAGGGCGT GGGCTGGCGTGAAGCTGCCACGGGCGCGTGGACGAGATGGCGGCCGTCTA CAAGGTGGCGCCGATGACGATGGGCTGGTGCCTGGAGTGCCATCGCCTGC CGGAGCCGCACCTCCGCCGCTCTCCGCGATCACCGACATGCGCTGGGAC 20 35 CCGGGGGAGCGAGGATGAGCTCGGGGCGCAGCTCGCGAAGGAATACGG GGTCCGGCGCTCACGCACTGCACAGCGTGCCATCGATGAACGATGAACA GGGGATCTCCTTGAAAGACGCAGATGAGATGAAGGAATGGTGGCTAGAAG 40 ATCGAGAGCCCGGGGCGCGCGCGCGCGGGGGGAACCGCCCCGGGG 25 CGTGGACGAGCCGGCGGGGCGTCAGCCGCGCGCGCGCTGCTCAAGCTGCTCG GCGCGAGCATGGCGCCGCGCGCGCGCGCATGAGCCC 45 GAGAAGATCCTGCCGTACAACGAGACCCCGCCCGGCGTCGTGCCGGGTCT CTCCCAATCCTACGCGACGAGCATGGTGCTCGACGGGTATGCCATGGGCC 30 TCCTCGCCAAGAGCTACGCGGGGCGGCCCATCAAGATCGAGGGCAACCCC

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		GCGCACCCGGCGAGCCTCGGCGCGCGCGTCCACGAGCAGGCCTCGAT
10		CCTCTCGCTGTACGACCCGTACCGCGCGCGCGCGCGCGCG
		AGGTCGCGTCGTGGGAGGCGCTCTCCGCGCGCTTCGGCGCGACCGCGAG
		GACGGCGGCGCTGGCCTCCGCTTCGTCCTCCAGCCCACGAGCTCGCCCCT
	5	CATCGCCGCGCTGATCGAGCGCGTCCGGCGCGCGCGCGCG
		TCACCTTCTGGTCGCCGGTCCACGCCGAGCACGCGCTCGAAGGCGCGCGG
		GCGGCGCTCGGCCTCAGGCTCTGCCTCAGCTCGACCAGGCCGA
20		GGTGATCCTCTCGCTGGACGCGGACTTCCTCGCGGACATGCCGTTCAGCG
		TGCGCTATGCGCGCGACTTCGCCGCGCGCGCCGCGCGCGAGCCCGGCG
	10	GCGGCCATGAGCCGCCTCTACGTCGCGGAGGCGATGTTCACGCCCACGGG
		GACGCTCGCCGACCACCGGCTCCGCGTGCGGCCCGAGGTCGCGCGCG
25		TCGCGGCCGCGTCGCGGGGAACTCGTGCACGAGTCTTTGTCTTGCGC
		CCTGTCCGGGAATAACGGACACCTTATCGCGGGTCGCTCTTTGTGCGCGG
		CTTCTGTACCTCTCAGGACAGGTAGAAGAGGGACTCAGGGGCCCTTATGT
	15	TAACTGGGGATGCCTTCGGGACGGCCGCAAATATATCCTATCACCTCACT
30		GGGTGTGGGGGAGCACCGCGAGGATGTACAACCTCTGTAACTCTATGTGA
		GATAATGTGTGCAGTGATCTGAGACTTATTTGTGTGACCGAGACGTCTCT
		${\tt CTTATTGGTACGCATAGTATAATATAACACGTCTCATACATA$
35		ATATCCGCGGTATGCGCGCACATAGAATAGGTGATGATAAATCCCTAGTG
	20	TGTGGAACTAGAAGATGCGGGAGTTACCTGATATTTACGGAAAAAGTATT
		ATCTCAACTACCTCTGTTGAGACTATCACTTCGGTGTCGTTGTGCTGC
		TGGT,

or its complementary strand,

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(b) DNA-sequences which hybridise under stringent conditions to regions of DNA-sequences according to (a) encoding proteins or to fragments of said DNA-sequences,

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5 181 .

(c) DNA-sequences which hybridise to the DNA-sequences according to (a) and (b) because of a degeneration of the genetic code,

- 5 (d) allele variations and mutants resulting by substitution, insertion or deletion of nucleotides or inversion of nucleotide segments of DNA-sequences according to (a) to (c), wherein the variations and mutants offer isofunctional expression products.
- 20 10 11. Peptide encoded by a DNA sequence according to claim 10 selected from the group consisting of

25 Seq ID No 83 >Contig56_003 2890 amino acids MW=307428 D pI=5.76 numambig=13

15 IRPRAAAVPMRSTVTGGVIAGPELGASYWADNLRQPVRFAAAAQALLEGGPALFIEMSPH
PILVPPLDEIQTAAEQGGAAVGSLRRGQDERATLLEALGTLWASGYPVSWARLFPAGGRR
VPLPTYPWQHERCWIEVEPDARRLAAADPTKDWFYRTDWPEVPRAAPKSETAHGSWLLLA
DRGGVGEAVAAALSTRGLSCTVLHASADASTVAEQVSEAASRRNDWQGVLYLWGLDAVVD
AGASADEVSEATRRATAPVLGLVRFLSAAPHPPRFWVVTRGACTVGGEPEASLCQAALWG

20 LARVAALEHPAAWGGLVDLDPQKSPTEIEPLVAELLSPDAEDQLAFRSGRRHAARLVAAP
PEGDVAPISLSAEGSYLVTGGLGGLGLLVARWLVERGARHLVLTSRHGLPERQASGGEQP
PEARARIAAVEGLEAQGARVTVAAVDVAEADPMTALLAAIEPPLRGVVHAAGVFPVRHLA
ETDEALLESVLRPKVAGSWLLHRLLRDRPLDLFVLFSSGAAVWGGKGQGAYAAANAFLDG
LAHHRRAHSLPALSLAWGLWAEGGMVDAKAHARLSDIGVLPMATGPALSALERLVNTSAV
25 QRSVTRMDWARFAPVYAARGRRNLLSALVAEDERAASPPVPTANRIWRGLSVAESRSALY

ELVRGIVARVLGFSDPGALDVGRGFAEQGLDSLMALEIRNRLQRELGERLSATLAFDHPT
VERLVAHLLTDVLKLEDRSDTRHIRSVAADDDIAIVGAACRFPGGDEGLETYWRHLAEGM
VVSTEVPADRWRAADWYDPDPEVFGRTYVAKGAFLRDVRSLDAAFFAISPREAMSLDPQQ
RLLLEVSWEAIERAGQDPMALRESATGVFVGMIGSEHAERVQGLDDDAALLYGTTGNLLS

30 VAAGRLSFFLGLHGPTMTVDTACSSSLVALHLACQSLRLGECDQALAGGSSVLLSPRSFV

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AASRMRLLSPDGRCKTFSAAADGFARAEGCAVVVLKRLRDAQRDRDPILAVVRSTAINHD GPSSGLTVPSGPAQQALLRQALAQAGVAPAEVDFVECHGTGTALGDP1EVQALGAVYGRG 10 RPAERPLWLGAVKANLGHLEAAAGLAGVLKVLLALEHEQIPAQPELDELNPHIPWAELPV AVVRRAVPWPRGARPRRAGVSAFGLSGTNAHVVLEEAPAVEPVAAAPERAAELFVLSAKS AAALDAQAARLRDHLEKHVELGLGDVAFSLATTRSAMEHRLAVAASSREALRGALSAAAQ GHTPPGAVRGRASGGSAPKVVFVFPGQGSQWVGMGRKLMAEEPVFRAALEGCDRAIEAEA 15 GWSLLGELSADEAASQLGRIDVVQPVLFAMEVALSALWRSWGVEPEAVVGHSMGEVAAAH VAGALSLEDAVÁIICRRSRLLRRISGQGEMALVELSLEEAEAALRGHEGRLSVAVSNSPR STVLAGEPAALSEVLAALTAKGVFWRQVKVDVASHSPQVDPLREELIAALGAIRPRAAAV 20 10 ${\tt PMRSTVTGGVIAGPELGASYWADNLRQPVRFAAAAQALLEGGPALFIEMSPHPILVPPLD}$ EIQTAAEQGGAAVGSLRRGQDERATLLEALGTLWASGYPVSWARLFPAGGRRVPLPTYPW QHERYWIEDSVHGSKPSLRLRQLRNGATDHPLLGAPLLVSARPGAHLWEQALSDERLSYL SEHRVHGEAVLPSAAYVEMALAAGVDLYGTATLVLEQLALERALAVPSEGGRIVQVALSE 25 EGPGRASFQVSSREEAGRSWVRHATGHVCSGQSSAVGALKEAPWEIQRRCPSVLSSEALY 15 PLLNEHALDYGPCFQGVEQVWLGTGEVLGRVRLPGDMASSSGAYRIHPALLDACFQVLTA LLTTPESIEIRRRLTDLHEPDLPRSRAPVNQAVSDTWLWDAALDGGRRQSASVPVDLVLG 30 SFHAKWEVMERLAQAYIIGTLRIWNVFCAAGERHTIDELLVRLQISVVYRKVIKRWMEHL VAIGILVGDGEHFVSSQPLPEPDLAAVLEEAGRVFADLPVLFEWCKFAGERLADVLTGKT LALEILFPGGSFDMAERIYRDSPIARYSNGIVRGVVESAARVVAPSGMFSILEIGAGTGA 20 ${\tt TTAAVLPVLLPDRTEYHFTDVSPLFLARAEQRFRDYPFLKYGILDVDQEPAGQGYAHQRF}$ 35 DVIVAANVIHATRDIRATAKRLLSLLAPGGLLVLVEGTGHPIWFDITTGLIEGWQKYEDD LRIDHPLLPARTWCDVLRRVGFADAVSLPGDGSPAGILGQHVILSRAPGIAGAACDSSGE SATESPAARAVRQEWADGSADVVHRMALERMYFHRRPGRQVWVHGRLRTGGGAFTKALAG DLLLFEDTGQVVAEVQGLRLPQLEASAFAPRDPREEWLYALEWQRKDPIPEAPAAASSSS 40 25 ${\tt AGAWLVLMDQGGTGAALVSLLEGRGEACVRVIAGTAYACLAPGLYQVDPAQPDGFHTLLR}$ DAFGEDRICRAVVHMWSLDATAAGERATAESLQADQLLGSLSALSLVQALVRRRWRNMPR LWLLTRAVHAVGAEDAAASVAQAPVWGLGRTLALEHPELRCTLVDVNPAPSPEDAAALAV 45 ELGASDREDQVALRSDGRYVARLVRSSFSGKPATDCGIRADGSYVITDGMGRVGLSVAQW MVMQGARHVVLVDRGGASEASRDALRSMAEAGAEVQIVEADVARRDDVARLLSKIEPSMP PLRGIVYVDGTFQGDSSMLELDARRFKEWMYPKVLGAWNLHALTRDRSLDFFVLYSSGTS 30

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LLGLPGQGSRAAGDAFLDAIAHHRCKVGLTAMSINWGLLSEASSPATPNDGGARLEYRGM EGLTLEQGAAALGRLLARPRAQVGVMRLNLRQWLEXXXXXXXXXXXXXXXWYNLLIIIQYTK VPFQGPFRML*

Seq ID No 84

>Contig56_027 700 amino acids MW=80569 D pI=7.02 numambig=0

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IQLNEHWKKDKKILILSFSPDDSQIIGFRSMLKPFTGSFNLARAATRLLWRYAMLMEIAS
YISSHYKLSSQISSETLLNEHLKKWNSAQGDILRKCRLVAKEYLDENNPEESIGDLQFNL

10 NISEIENNIVSLLERSDRKVVILMDKLDEAYEPDNIGIGIIAGLAYASIELNQKAKCIRP
IIFLRDNIFRSLSKEDPDYSRNIEGQVIRLHWDWAQLLMLSAKRMKVAFKLDIEKDQRVW
DRCTADDLKGRNGFKRCLQFTLYRPRDLLSLLNEAFFSAFRENRETIINTDLEYAAKSIS
MARLEDLWKEYQKIFPSIQVITSAFRSIEPELTVYTCLKKIEASFELIEENGDPKITSEI
QLLKASGILQSLYSVGFVGIRDKNTSSYSFCHDGRTPDKGFESNEKLLIHPCYWLGLNLN
15 RNALAPEEAEEINDEYDINIISDNSAIRNKTIGQITTHLDQIPIGNEGATEFEQWCLDAL
RIVFASHLTDIKSHPNGNAVQRRDIIGTNGGKSDFWKRVLEDYKTRQVVFDAKNFEELGP
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35 Seq ID No 85

>Contig57_001 372 amino acids MW=38411 D pI=12.39 numambig=10

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RVRPWGGLRYGRAQTALRRPATRRSDLGSDPGFGHESGWPVDRVDGTQCARSGGALARGA

25 AERSRRRGHRLCRDPRNGDLARRPDRGRGAACRVGAGAGRWEPLRAGRSEDKPRPPGGR

CRRGGFDQGGAGSAPRTDPAKPPFPHAQSADPDRGDRARAGDGAGAVAAGGPTALRGGER

VRFQRHQRPCRAGGGAGHGARTGDAGALSGAFGAVGEERRRAGRTGGAALSAHRRVPGAG

45 SRRRVQPGIDA*

LQKLRNPEKHDAIDRQMGKLLTLYETSYMAIKSTQKKRRK*

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Seq ID No 85 >Contig57_002 2259 amino acids MW=238258 D pI=5.92 numambig=0 10 ${\tt MSYTLGLQGPCLTVDTVCSSSLVAIHLACRSLRARESDLALAGGVNMLLSSKTMIMLGRI}$ QALSPDGHCRTFDASANGFVRGEGCGMVVLKRLSDAQRHGDRIWALIRGSAMNQDGRSTG LMAPNVLAQEALLREALQSARVDAGAIGYVETHGTGTSLGDPIEVEALRAVLGPARADGS RCVLGAVKTNLGHLEGAAGVAGLIKAALALHHELIPRNLHFHTLNPRIRIEGTALALATE 15 PVPWPRAGRPRFAGVSAFGLSGTNVHVVLEEAPATVLAPATPGRSAELLVLSAKSAAALD AQAARLSAHIAAYPEQGLGDVAFSLVSTRSPMEHRLAVAATSREALRSALEVAAQGQTPA GAARGRAASSPGKLAFLFAGQGAQVPGMGRGLWEAWPAFRETFDRCVTLFDRELHQPLCE 20 10 VMWAEPGSSRSSLLDQTAFTQPALFALEYALAALFRSWGVEPELVAGHSLGELVAACVAG VFSLEDAVRLVVARGRLMQALPAGGAMVSIAAPEADVAAAVAPHAALVSIAAVNGPEQVV IAGAEKFVQQIAAAFAARGARTKPLHVSHAFHSPLMDPMLEAFRRVTESVTYRRPSIALV SNLSGKPCTDEVSAPGYWVRHAREAVRFADGVKALHAAGAGLFVEVGPKPTLLGLVPACL 25 PDARPVLLPASRAGRDEAASALEALGGFWVVGGSVTWSGVFPSGGRRVPLPTYPWQRERY WIEAPVDREADGTGRARAGGHPLLGEVFSVSTHAGLRLWETTLDRKRLPWLGEHRAQGEV VFPGAGYLEMALSSGAEILGDGPIQVTDVVLIETLTFAGDTAVPVQVVTTEERPGRLRFQ 30 VASREPGERRAPFRIHARGVLRRIGRVETPARSNLAALRARLHAAVPAAAIYGALAEMGL QYGPALRGLAELWRGEGEALGRVRLPEAAGSATAYQLHPVLLDACVQMIVGAFADRDEAT PWAPVEVGSVRLFQRSPGELWCHARVVSDGQQASSRWSADFELMDGTGAVVAEISRLVVE ${\tt RLASGVRRRDADDWFLELDWEPAALGGPKITAGRWLLLGEGGGLGRSLCSALKAAGHVVV}$ 20 35 ${\tt HAAGDDTSTAGMRALLANAFDGQAPTAVVHLSSLDGGGQLGPGLGAQGALDAPRSPDVDA}$ DALESALMRGCDSVLSLVQALVGMDLRNAPRLWLLTRGAQAAAAGDVSVVQAPLLGLGRT IALEHAELRCISVDLDPAEPEGEADALLAELLADDAEEEVALRGGDRLVARLVHRLPDAO RREKVEPAGDRPFRLEIDEPGALDQLVLRATGRRAPGPGEVEISVEAAGLDSIDIQLALG 40 ${\tt VAPNDLPGEE1EPLVLGSECAGRIVAVGEGVNGLVVGQPVIALAAGVFATHVTTSATLVL}$ 25 PRELGLSATEAAAMPLAYLTAWYALDKVAHLQAGERVLIHAEAGGVGLCAVRWAQRVGAE VYATADTPENRAYLESLGVRYVSDSRSGRFVTDVHAWTDGEGVDVVLDSLSGERIDKSLM 45 VLRACGRLVKLGRRDDCADTQPGLPPLLRNFSFSQVDLRGMMLDQPARIRALLDELFGLV ${\tt AAGAISPLGSGLRVGGSLTPPPVETFPISRAAEAFRRMAQGQHLGKLVLTLDDPEVRIRA}$ PAESSVAVRADGTYLVTGGLGGLGLRVAGWLAERGAGQLVLVGRSGAASAEQRAAVAALE 30

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AHGARVTVAKADVADRSQIERVLREVTASGMPLRGVVHAAGLVDDGLLMQQTPARFRTVM GPKVQGALHLHTLTREAPLSFFVLYASAAGLFGSPGQGNYAAANAFLDALSHHRRAQGLP 10 ALSIDWGMFTEVGMAVAQENRGARQISRGMRGITPDEGLSALARLLEGDRVQTGVIPITP ${\tt RQWVEFYPATAASRRLSRLVTTQRAVADRTAGDRDLLEQLASAEPSARAGLLQDVVRVQV}$ SHVLRLPEDKIEVDAPLSSMGMDSLMSLELRNRIEAALGVAAPAALGWTYPTVAAITRWL $\verb|LDDALVVRLGGGSDTDESTASAGSFVHVLRFRPVVKPRARLFCFHGSGGSPEGFRSWSEK|$ 15 SEWSDLEIVAMWHDRSLASEDAPGKKYVQEAASLIQHYADAPFALVGFSLGVRFVMGTAV ELASRSGAPAPLAVFTLGGSLISSSEITPEMETDIIAKLFFRNAAGFVRSTQQVQADARA ${\tt DKVITDTMVAPAPGDSKEPPVKIAVPIVAIAGSDDVIVPPSDVQDLQSRTTERFYMHLLP}$ 20 10 GDHEFLVDRGREIMHIVDSHLNPLLAARTTSSGPAFEAK* Seq ID No 87 >Contig57_027 419 amino acids MW=46737 D pI=5.09 numambig=0 25 MTQEQANQSETKPAFDFKPFAPGYAEDPFPAIERLREATPIFYWDEGRSWVLTRYHDVSA 15 VFRDERFAVSREEWESSAEYSSAIPELSDMKKYGLFGLPPEDHARVRKLVNPSFTSRAID LLRAEIQRTVDQLLDARSGQEEFDVVRDYAEGIPMRAISALLKVPAECDEKFRRFGSATA 30 RALGVGLVPQVDEETKTLVASVTEGLALLHDVLDERRRNPLENDVLTMLLQAEADGSRLS TKELVALVGAIIAAGTDTTIYLIAFAVLNLLRSPEALELVKAEPGLMRNALDEVLRFDNI LRIGTVRFARQDLEYCGASIKKGEMVFLLIPSALRDGTVFSRPDVFDVRRDTGASLAYGR GPHVCPGVSLARLEAEIAVGTIFRRFPEMKLKETPVFGYHPAFRNIESLNVILKPSKAG* 20 35 Seq ID No 88 >Contig57_043 492 amino acids MW=52617 D pI=11.54 numambig=0 MAARARKSCRARGSRPAPMRTSPPTSTPTPRPRGWRWTSFTSRRPSASRPAASGSSSGSV 40 RAPSPRGNGSECSTTTLPAEEASWPRRPCRMPTSSCSSPSRSRAALSLHLLPPSSGRRPS 25 GNIALSAALSPPAGPRALPRSPSPSYHPCVLLQRRPRRSNRRAGAALRARQESVLARPAH RWKDRRSMEKESRIAIYGAIAANVAIAAVKFIAAAVTGSSAMLSEGVHSLVDTADGLLLL 45 LGKHRSARPPDAEHPFGHGKELYFWTLIVAIMIFAAGGGVSIYEGILHLLHPRQIEDPTW NYVVLGAAAVFEGTSLIISIHEFKKKDGQGYLAAMRSSKDPTTFTIVLEDSAALAGLTIA

FLGVWLGHRLGNPYLDGAASIGIGLVLAAVAVFLASQSRGLLVGESADRELLAAIRALAS

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ADPGVSAVGRPLTMHFGPHEVLVVLRIEFDAALTASGVAEARERIETRIRSERPDVKHIY VEARSLHQRARA*

12. DNA sequence according to any of claims 1 to 5 wherein the DNA is selected from the group consisting of

(a) the following DNA sequences:

Seq ID No 89 (>Contig10)

10 GGTAGTGAAATATGCTGTATTCAACAGAAAGCTTGATGAATTGATCTAGA

 AAGTAGAGCGAGAGAATCAAGTAAGATAGTAGGATGCATTATAAATATAG
 AATATATACTGCATACGATGACAGCATGCGCACGAATAGAATGCATAAGA
 GGCAAGCCAATAACCAAAAGTGGAGCCAGAGGAGATAGTCTCGCCAGTAG
 AAATAATGCTCAGCCAAGCGAGGTTGGACATATCAGTTCCAGAGTAGGTC

 15 TCAACCCCGTATATGAGTCCAATGAAGCCTGTCTCATCCAGTTAACGGCC
 TTTTGAGCAGAGAATCCTCCCTATTTTCGGAGAGGACGCGTCGAATATAA

AGCAGGCAGAGAATCCTCCCTATTTTCGGAGAGGACGCGTCGAATATAA
AGCAGGTCCAAAGAAGCAAGCAATAGCCAAAAGTTTGAAAGGTTAGTACG
AGCAGCGGCTGGAGGACACTATGGTCGTGCAACGGGGGTAAAGGGTTTCA
CGTATTGTAGCAGAGCACGTCAGAGGGTTATTCGTGACATTCGAGGCCAA
CGAGGCGGTAGGACTTCGTAAGCGCATGACCATCCCGGTCACAAACGTAG

30 TCTCCGGGGGCGCGTCGTCCGGGGGGCGAGGCGTCGAGGAGCTCCGGC

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GCGAACGCGACGTGGCGCTCGCCGAGCGCGCCCCGAGAAAGGCGCGCCG GCACTCCCTCCGGCGGACCTTCCCGCTCGACGTCTTCGGCAGCGCGCCCCG 10 GCGCGATCAGCGCGACGGCGTGCGCGACGAGCTGGTGCTCGGCGGTCACC GCCTCGCGCACGCCCACGATCTCGCGCGGATCCGCGGCCACGCGCGG GTCGACCTCGCACACCACGGCGAGGCGCTCCTCGCCCTCGTGCTCCACGG AGAACGCGGCGCTGCAGCCCGGCCGGACGCGCGATGGCTGCTCTCGACG 15 GTCTTCTCGATGTCCTGCGGGAAGTGGTTGCGGCCTCGAAGGATGATGAG GTCCTTCGACCTCCCCACCACGAACAGCTCGCCGCCCCGGAGGAAGCCGA 20 CCGAACGTGGCCTCCGTCTCCTCCGGGCGCCCCCAGTAGCCGACGGCTAC 10 GCTGGGCCCGGACACCCAGATCTCCCCGATCTCCCCCGGCCCGAGCTCGT TCCCCGCGGGATCGACGACCGCCCGCGGATCGAGCGCCCGACCG 25 GAGCTCCACCTCCTCGGGGGCGAGGCGCCCAGCACCGGCGCCTCGGCCC GCGCTCCGCCGCTCACGATGAGCGTGGCCTCGGCGAGCCCGTAGCAGGGA 15 30 ATCGAGCGTGTCGGCGCGCCCGCGCCCCGTGAACGCGACCTCCC ACGACCGCAGATCGAGCGCCGCTCGCTCCTCCGAGCTCTTCCGGACG CACAGGTCGTATGCGAAGTTCGGGCCGCCGCTCACCGAGGCGCCGAGCGC 20 CGAGACGCGCGGAGCCACCGCATCGGCCTCTGCAGGAACGAGAGCGGCG 35 ACATGAGCGCGACGCGGATCCGCCGGTAGAGCGCCTGCAAGATCCCGCCG ATGAGCCCCATGTCGTGATACGGCGGCAGCCAGATCACCCCGACCGGATC CGGGCTCGTCAGGTCGAATCCATGCGCGATGAGCCGCGAGTTGTGCAGCA GATTCCCGTGGGTGAGCATCACCCCCTTGGGCTCGCCGGTCGAGCCGGAG 40 CTCGATCGGGCCCGGCGACGGGCCGTCGGTCGCGATCCACCGGAGCCGCT GCAGCGCGGCGCCGCGCGCGCAGGACGCCACGATGCCGGCG 45 ACGGCCGATGACGTGAGCGCCGCCTCGGCGCGCGCGTCCGCGACGATGGA AGCGACGCGCGGCGGCCGAGATCCGGCGGATAGG CGGGCACGGTCCGGACTCCAGCGTAAAGACACCCGAAGAACGCGGTGATG

TACTCGATCCCCGGCGGATACAGCAGCGCGCGCGGGCCCCGGGGGCGAC GCCCGATGCCTGCAAGAGGGCCGCGCGCGCGCGCGCGCCCCAATTT . 10 CCCGCAGGGTCACCCAGGTCGCCCCGGCCTCGACGTCGCCGGACTCAAGA AAGCAATAGATTGGGCGGGCGGGGCTCAGCTTCGGCCCGCTGGCGCAAGAG GTCGATAACGGTGGAAGGGCGGTTCCGTTCCGTTCCAATGCAAGAA AAGCATCATTCATTGAACAGACCCCTCCGCCGCGGAGATAGCAGCTTGTC 15 CGCTGCGACACAACCGCCGCGCGACGCGCGTGGCACGGCGGGATCCGGGC TCGTGAACCACCGCCCACAGCGACACGCGCCCTGGCTCCGAGGGCGGCGT 20 10 CCACGTGGTCCCGTTGCCCCCGCGGGAGGCGCCGGTCGTATCGCTCACCA GGCGGCGCCCCGTCGAACTCGCCACCGTCCGTGTAATAGTCGACCCAG ATCGCCTCGCGCGGCGGTGGACCGCCGAGCCCGGCGGCTTCCTCGTCCAC CTCGGCGGCCTTCTCGGGCACGACAGCCTCAATCTCATAGGTCGTGCACT 25 CGTCCTCGGCCGGCTCGGCCGCCGCCAGCCTTGGGCCTGCTCCTCGGAC 15 CGAACGCACCGCTTCACGACGGCCAAACCGTCCTCGCCCGGCGCGCCACCTC ATTGCCATCGAGCTTCAGCGTGAAGCCGTCGATGGGCGGGTTCGTGTTCA 30 GCCGCTCCTTCTTGAAGACATAGACCTGCGTGTAGCCCACGACGAAGCTG TCCGGACCGAGCACCGTCCCGTCGCCGACGCACTCCAGCGGAAACCC GGCCGTTTCGGGCGCCGAAGCCACGCGTGTCGTGCCGGCGCACACGGCGA ACAGCACGTAAGCCGACGAGTACACCGTCCCCGTCTCGGTGGGCCTCGCG 20 35 TCCTTGAGGATCTCCTTGGGCAGCTTCCACCCGAACGAGACCGCATCGGG CTCGCCGCTCTTCTCCGGACCGATCTCCTGCTGCGCGAAGGGGACGGTGC CCGCTGGCACCGCCGCCGCCGCCACCATTGCCGCCTTC 40 25 GCCGCCTCCAGCGCCACCACTGCCGCCGTCGCCGCCGCTGCCACCATCGC CGGATTCGCGACGATTCCCACCGCATAGGTGCCCAGCCACTGCGGGATGC 45 ACCCGAGGTGCTCGTCCACCCGGACCGGCGGATTCACGCAGCCGCCCACC CACGTGACCTCCGCGCGCGCGCCCCCCCCCCCCCCTTCCGCGTC GGCGTACGTCATCCGGAACGTCACGAGCTCTTCCGCCGCCGCGTACGGCT

50

TGTCCGCCGTCACGGCGAGGACGCGGAGCCCCTTCACCTCGGACGAAGGG GCCATGTCGCTCCCGGCGCAGCAAGGGATGCCCACGGCCAGGGTCGAGAG 10 CGCGGCCAGCGCGCGACGAGCGGGCAGTGCGGTCCGTTTCATCAGAA ATCTCCTCGCAGCCCGAGCGTGGGCAGGAAGGGGAGCCCCGTCACGTACT CCCGCTTCGTGTAGTTGAAGTTGTAGCTGATGCCCTCCGCAGCCATGTAA 15 TTGTAGACGTTCTGGATATCGAGGTAGAGCCCGAGCTGCCACCTCTTGAA TTTCCACGTCTTGTCGGCGCGGATGTCGAGCTGGTGAAACAGCGGCATCC GCTCGCTGTAGTCACCCCCGAGCGGGATCGGCGAATACCTCGCCGAGGAC GCGTGGTAGATCGCGTTCACCCGGTTCGGATTGCACCCCTTCTCCTCCGG 20 10 ATCGCAGACATAGGGCGTCTGCAGGTTGCCCGACACGAGCCGGAAGCGCG CGCCCAGCTCCCAGCCCCGGCCGAGCCGCAGGCTCCCGAGCACCGTCAGC ACGTGCGTCTGATCGAACTGGGTGAGGTGCTCCTCCTCGTCGGGGCCGTC CTTGCGCACCGACGGGGGGGGGTGTACGCCGCCCAGCCGAAGAAGCGCT 25 CGTCCGGCTTGTACTTCAACAAGAGCTCGCCGCCGACCGCGTATCCGGTG CCATCGTTGGCATAGTCGTCCTTCTCCGGCGAGAAGACGACCAGCCGATC GAGCTGCTTGTAGAACCCGTCCAGCGTCACCTCGATCTGCGGCGTGATCT 30 CCTGCTCCACGCCGAGGCCGTAATGCACGGCGCGGTTCGACTTGAGCTCC GCATTGCCGAACGGCTCGATGCTCTCCGCGAACTGCGGCGCCTGATAATA AAGGCCCACGCCCCCTTGGCCGTCGTCCGCGGGAAGCCGCTCCGGATGT CGTAGCGCGCGTTGACCCGCGGGCTCACGTCGAGCGTCTGCGTATCGAGC 20 35 GACCTCGAGCTCGGCATACGCCGCGGGCCGCGAGTACGCGCCGTCGAACG ACCGATCCTGGAACGGGTACGTCGAGAACGGCTGGTTCGACGGGTGGCCC GCGGGCTGCTGCGACGCGCGCGGGATGTTGACCGTGGCGACGCCGCCCGA 40 25 GAGGTCGGTGCCGACGTTCATCGTGAGGTACCGCGCGAACCTGTGCGAGA GCTCCAGCCGCAGGTCGAGCGAGGTCGAGACGTTGAAGGCGAGGGGA CAGATCTCGAAGTCGGCGATGTCCCGGCCGAGCGCCATCGACCACAGCAG 45 AGGCGGTGTGCAGCCCGAAATCGCCCGTCAGCGCCGGCTCGTCCTCCGGC GGCTTGTCCAGGGTGATCTTGAAGGCGTCGTCCGATCCGTAGAAGCTCGC 30

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GCGCACGCGCTCGCGGAGGGGCGCCCTCGAGGACGAACTGGTAAT CATAGTAGACGGGCGCCTGCGTGACGCTGGAGCCCGCCTCCTTGAGCACG 10 GGCCCGAGCCACGCGTCGACCCAGCTGCGGCGGCCCGCCGCGATGAACGT CCAGTCCTTGAGGAACGGGACGGGGCCCTCGAGGAGCACGCGCCCGTCGA TGAGGTCGAGCTGGACCACGCCGTGGTACTTGCCGTCCTGCTTCGGCGAG CGGAGCCCGACGTCGACGATGCCGCCCCATGGCGCGCCGTACACGGCGCT 15 CCGAGGAGAGCCGCCGAAGTGGTAGATGATCGGCACCGGGGTGCGATCG ACGAACGTGAGCGTGTCCTGGGGCGCGGACCCGCGCACGATGAGCAGCCC 20 10 GAAGCCGCTGCGCGCGACGCCCGGCAGCCTCTGCAGCGACCGCAGCGCGT CGCCGCCGGTGCCGGGGATGCGGTCGATCTCGCGGCGCTCGATCGTCCTC CGCGTCACCTCGCGCGGGGGGCGCTCGCCCTGCACGGTCACCTCGATGCC CGGCGCCTTGCCGTCCTGCGGCGCGCGAGCGAGATGCGGTAGCGCACCT 25 CGATCGCCTCGCCGGCCGATCTCCTCCTCGGCGGCGAACGGCTCGAAC 15 GGCGCACGAGGGTGACCGCGATGTCCGGGGAGCGGCTCGCCGGTGCCCGCG 30 GGCCGCATCGGCGGGCTTGGGCGTGAGCGTGAACGCGTACCGGTAGAGGA 20 35 AGGCCGGGCGCGCGAGCGCCGCCTCGTTGAAGCCGTGCCCGCCGG GCGTCGCGACCTCGGCCTTGGTGACGCCCCGGTCTTGTCGATGTCGAGC TTGAGGATGACGCTGCCCTCGACGCCGGCGCGCGCTCGATCGGATA 40 25 CCGGCGGGGGCGCCGGCTGAGGGACGACGCCGCCGCCGCCGCCG CGGGGGACCGAGGCGCCCGAGTCGCCCTCGGCGCAGGAGGAGGCTC 45 CGACCGCGAGCAGCGCTTCCGAGACGACGAGGCCCATCACGGAGGAC GCTGTGGAAGGCATGCGGCCCGCCCTCTCGCATGGCGAGGCCGAGGCGGA ${\tt AAGACGCATCGCGCAGCCAGGACCGTGCTTCACATTGCTTCACACAACGG}$

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CGGGCGCGCGATCGCGAGCGCGCGCGGTGCGATCAGCCGCCGACCTCG GCCACGAACCGGCTCACGTCGTCGCTGTCGCCCACGAGCAGCAGCGTGTC GCCGTCGCGGATCACGTAGTCCGGTGTGGGCGCCTCGAGCCGCGGCTTGT CGCCGGGCCGCTTGTTCGTGTGCGGCCGCACACCGAGCACGTTGATGCGG TACCGCTGGCGGATCTTCGAGCCGGCCAGCGTCTGCCCGACCAGCGGCCC GTGGGCGTTCCAGGGGACCACGCGGTAGTGGCTCGCGAGGTCGAGGAGGT CCTGCGCGAGCGGCATGGTGATGTCGGCGCCGACGCGGCCGATCTCG GTCTCGAGCTGGATGACGCGGGTCGCGCCCCACCGCGCGCAGGATGTCGGC CTGGCGATCGGTGGCGCGCGCGCGATGATCTCGCGCACGCCCATCCGGA 10 CGAGGGAGGCCACGCAGAGCACGGACGGCTCGAAGTGCTCGCCGAAGGTC ACGATCGCGGTCTCCACGTACTGCGCGCCGATCCCCTCGAGCACCTTGTG GACGGTGGCGTCGCCGACGAACGCGGCCGAGGTCTTGTCCTTCACGGCGT CGACGGCCTCCGGGTTGTTGTCGACCGCGATCACCTCGGCCCGGTTCTTC 15 CAGAGGGTCTCGACGACCGACGTGCCGAACCGCCCGAGCCCCGATGACGA GCGGCGCGCGAAGGTCTCACGGATGCGCCGGGAGCGCCACGGTTCGGCG CAGTAGAGCTCGTCCTGGTGCTGCCACCGCTCCGAGATCCACGCCTTCAG 20 GTACGCGATCTCCTCCTCGTACGTCGTGAAGTCGTCGCGCCAGCTCCAGC CCTCGTAGCTCCGGTACGCCTCGCCCCACCGCGCCTCGTCCCGGCGCGCG .CTCGCGTCGATGCGCTCCACGTAGCCGTCCACGATCGCGTGGATCTCGGC CTCGGCGAGCGCGCGCGCAGGACCTGATCGTAGCGGGCGCGCAGCGGGT CGCCGATCGACGGCTCCTCGAGGAGGCGCTCGAAGAGGAGGTTCACGTCG 25 CGGTAGTCGACGCGACGCCGGCTCGCGTCTCCCACGACTG GCCGAAGCTCGCGTTGAAGTCCCACGGCGCGTAGCGGAATACGCCGTCCG CGGCCGGATCGCGGTAGTGGTAGCTGTTCTTTCCGGCCGAGTCGTTGGCC ACGATGAACGTGACGAAGATCCACCAGTCCTCGTAGTCGCGCAGATCGAT CCGCGACCCGATCTCGGCGGCGAACGTGGCGTCGTCGGACTCGGCCACGA 30 AGCTCACGAGATCTTCCAGATCCGAGAACGCCTCCGGCTCGCCCTCGGCC

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GGCGCCCCTTCCTTCTCGAAGCCGTCGTGCAGCGTGTCCTTGGGGTC GCCGGACCGGTCGGTCAGCGCGAAGTTCGCGTCGTGGCTGACCGCCTTGT AGAGGTTGCCGTCCTGCGGGTAGCCGTGGTCCTCCATCAGGTAGCCGTCG ACGTGATCCGCGACGGTGTAGAGCCCCGCGTACTCCCCGTCGAGGTACAG GACGGCGCTGTAGGTCTTGATCTGGATGTGCTCGGGATCGAGGCGGTTCC ${\tt AGAGGTCATAGGCGAGGCGCTGCCGGACATAGGAGTTGTCGTCGAACGTC}$ CTCGTTGAACTTGTCGTCCTTGGGGAACTTGAGGGTGTAGCTCCGCTTCG GGTACGAGAGCGAGCTCTCGCCGCGGAGCTCCGCGCGCGTACGTG $\tt TGGCCGCGGTAGATCACCGTGGCCGGGGCGTACTCCTTGTCCTCGGGGAC$ GGGCGAGAGGAGGAGCACCGGCAGGCCGTACTCCTCGGGGTAGCGGGTCG GATCGACGGCCACGTTCGACGGATCGGCGAAGGCGTCGGCGACGCCG ACCTTGACGCGCCCGACCTCGGACGTCTGCGCGACGCGGATCTCGATGTC ${\tt TCGGGTCGTACGCGGCGCCCTCGGGGGGGGGGGGGCCGACCTCGAACGCGTCG}$ CCGGCGAGCGCGAGGCCGCTCGCGCACGTCACCGGGAACGTCACGGTCTC CCCCTCGAGGAGCCAGTGCGGGCCGCCGCCCGACGGCTGGCAGCGCGAGC CCTCGGCGCTGGAGCCCGCCGCTGGAGCCGGAC

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TGTAATAAACAGGAGACAAGAGCGACTACATAAGAGAGCGAAGCGAATAG . 10 TAAAGCAACAAGACGGAGAGAGCGAAGCAGCAACGATTAGAAGAAA GACGACAGGAAAGTGAAAGCGAAAGAGAGCAGGTAGAAAGAGAACCAAAA AAGCACGAAGGAAAAGGAAGCTTCTATGATAGGTGCGGGACAAGGCGTAG 15 CTACAGGAGACAGCCGGCATACGAGGAGCCGGTAAAAGCTAGCCTTTCAG AACACATCGGGAGCGCGTAAAGGCGGACCACGCTCGACGGGATCATGTAC GCCGACAGCGACGCCTTCAGCCCCGCGCGCGCACGTCCGGCGCGCCCCGC CGCGTCGCCGTCGAGCACGACGTAGGCGACCAGGCGGCGTCGCCCGGCG 20 CGTCCTCGCGCAGGACCACGGCCGCCTGGCCCACGCCGGGCACGCGCCGG ATCTGCGCCTCGACGTCGCCGAGCTCGATCCGGTGCCCCCGGAGCTTGAT $\tt CTGGTGGTCCGAGCGGCCCTGGAACTCGAGCATCCCGTCGGGCAAGAAGC$ 25 GGGTCGGGCAGGAAGCGCTCCGCGGTGAGCCCGGGCTGCCCCACGTAGCC 15 GCGCGCGAGCGCCCCGCGATGTAAAGATCGCCGAGCGCCCGATGG $\tt CGGGGCGCGCATCGCGCCGTCGAGCACGAACACCTCGGCGTTCGCGACC$ 30 GGCGCCGAGGGGACCCACGTGACCCGCGGGTCGCTCGGCAGGACGCA GCCGGTCACCGCGATCGCGGCCCTCGCTCGGCCCGTACATGTTGATGAGGT CGCCGTCGTGCTTCGCGTAGAAGCGCCGGACGAGATCGAGCGGCACCGCC TCGCCGCCACGAGGACCTTCCGCAGGCTCGCGGGGAACGGCTGCTCGGG 20 35 CCCCCGAGGAACGCCGCGAGCATCGAGGAGGACGAAGTACGCGGTCGTCG CCCCCTCGTCGCGCACGAGGCGCCGAAGGTACTCGGGATCGCGGTGCCCG CCGGCCCGGGCGACGACGACGAGGGGCCAGAAGAT CTCCCAGACGGAGACGTCGAAGCCGAACGCGGCCTTGAGCAGGACCCGGT 40 CGTCCGCGGTGAGCGCCCAGTACCGCTGGATCCACTGCATCTGGTTGACG 25 ATGGCGCGGTGGGAGATGAGGCTCCCCTTCGGCGTGCCCGTCGATCCGGA CGTGTAGATGACGTACGCGCCGCTGTCCGGCGGCGGCTCACGGCGGCC 45 GCGCGTCGGAGCACGCGGCGATCTCGGCGGCGTCGAGGAGCAGC GAGGAGGCGCCCGCGCGTCCCGCATCATGAAGGCGAGGCGCTCGCCGG

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CCGGGCGCCCCCCCGGTCGAGCGCGCGGATCGCCCGCTGCTGCGG $\tt CGAGAGGCTGAAGCCGGTCATCTCGTGGTCATCCAGGTCGTCCTTC$ 10 TCCGCTCGAGCTCCCGGCGGCGCGCGCGCGCGCTCGAGCTCCCCCCGG AGCTCCGAGACCGGGGTGTCCGGCCGCCGCGCAGTGGCCAGGATCTG 15 ${\tt CCGGTAATCGCTAAGGAAATTGTCGACCGTCGCCCGGTACAGCTCGC}$ TGCTGTGCTCGACGCCGAAGCGGAACGAGCCGCCGGCCTCGGCGACCGTG AGGACGAAGTCGAACGCCGTCGTGGTCGCCTCGCCCTCCAGCGCCTCGAG 20 1.0 CTCGAGCCCCTCGAGCTTCATCGGGGGGGACGTGCACGTTGCGCATGACGA ACTTCGCGTCGAAGAGGGGCACGTGCCCGACGGCCCCCTTCGGCCGCAGG GCCTCGACGACCGGTCGAACGCCAGGTCCTGGTGCTCGAACGCCTCGAG CGCGACGTCGCGCGCGCGGGCCGGACGTCGGGTCGCCCC 25 CGCAGTCGGTCCGGAGCACGAGCTGGTTGACGAAGAAGCCGATCATCGGC 15 TCGGTCTCGACGCGGTTCCGGTTCGCGACGTCGCCCACGACGACGTC CTCGAGCCCGGTGCGCTGGTGCAGGACGAGCTTGTACGCGGCGAGCAGGG 30 CCATGAAGGGGGAGATCGCCTCCCGCTCGCAGAACGCCTTGATCTGGCGG GTGAGCTCGGCCCCGGCGTCGAGGCTCCGCCGCGCCCCCGCGCCACGTCCT CCGAGAGCTTCGTCGTCCAGTACCGGAGCTCGCCCTCCAGGACCTCGCCG 35 GACAGCCACGCCGGCTGGGCTGCGGCGAAGTCGACGTACTGCGCCGGGAG CTCCGGCAGCCGGGAAGGCTGGCCCTGCGCGAAGCCGCCGTAGAGCGCGG CGAGCTCGCCGACGAGACGCCGACCGACCAGACGTCGAACACGACGTGG TGCACGACGAGCGCGATGACGTGCTCGTCGTGGCGCTTCCGGATGACCCG 40 ${\tt CACGCGGAGGAGCGCCCGCGGCTCAGGTCGAACGGCGCGAGGCTCTCCT}$ ${\tt CGAGGACGAGGCCGAGACCGCCGCGTCGAGGGCCTCGCCCGCGAGGTGC}$ TCGAGGTCGGACATCCGGAACGGCACCCGGGCCTCGGGCGCGACGACCGG 45 GAACGGCACGCCGTCCCTGGCGCTGAACGTCGTCCGCAGCGCCTCGTGGC GCCGCGCGATCTCGAACAGGCTGCGGCGGAGCGCGTCGACGTCGAGCCGG $\tt CCCGTCGCGCGCACCACGAACGGGATGTTGTACGCCGGGCTGCCCGGCTC$

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GAGCTGATCGACGAACCACAGCCGGTGCTGCGCGAACGACAGCGGGAGCG GGCCGTCGCGGGGATCCGCGCGGGGGGAACTCGCGCCGCCGCGCC 10 TCGCCGCGCGCGCGCGTCGACCTGGGCCGCGAGCGCCGCGACCGTCGG CCCCTGGAAGAGCGCCCGCAGCGGGGAGCTCGACGCCGAGCTGCGCGCGGA TCCGGGACATCACCTGGGTCGCGACGAGCGAGTCGCCGTGCAGGCCGAAG 15 AAGTCGTCGTGGACGCCGATCTCGTGGACGCCGAGGAGGGCGCTCCCAGA TCGCGGGCGATCGCGCCTCGGACTCGGTCGACGCGCGCGAACGCGGC CCCGGCGTGCGCGGGAGACCGCCGACGTCGGGAGGGCGTTCGGCGCGG 20 10 CGCGGCGCGATCCAGTGCCGCCCCGCTCGAACGGGTACGTCGGCAAGCG GACGAGCGCCGGGGGACGCCCCCGCGGACGGCCGTCCAGTCGACGGC GTGGCCCGCCTCCCAGAGCTGGCCGAGGCCTCGGCCAGGCTCGCGGGCT CGGACGCGGCGTGGGTCGACCCGAGGCTCGCGATCGCGGCGCCGCCGCGC 25 CCGGCCAGCGTCTGCCGCACCAGCGTGGTCAGCCCGCGGCCGGGCCGAC CTCGAGGAACAGGGCGTGCCCGGACGCGAAGAGCGCCTCGACGCCGTCGC TGAAGCGGACCGGCTGGCGGAGGTGCCGCGCCCAGTAGGCCGGATCGGTC 30 GCCTCGGCGTCGGTGAGGAGGGGGGGGTGACGTTCGAGACCACGGGGAT CTCCGGCGGGAGAGCCGCGCGCGCGCACGCTCTCGAGGAACGGGGCCA CCGCGCCGTCGATGAGCGCGCAGTGGAACGCGTGGGACGTCTGCAGCGGC CGGGCGAACACCTCGCGCGCCTCGAGGCGCGCGGCGAGATCGCGGATCGC 20 35 GCTCGCCGGGCCCGCGACAACCGTGAGCTTCGGGCTGTTGACCGCGGCGA ACGGCCAGCATGCTCCCGGCCGGCGCCCCCTGCATGAAGCGCCCCCGATC GATGACCAGGGACATCGCGTCCTCGAGCGTGAACACGCCCGCGACGCAGG 40 CCGCCACGAGCTCGCCGAGGCTGTGGCCGATCATCGCCGCGGGCTCGATC 25 CCCCAGCTCATCCAGAGCCTGGCGAGCGCGAGCTCGACGGCGAAGAGCGC GGGCTGCGCCAGCGGGTGCCGAGCAGCGTGCGCCCTCGCCCT 45 CGCGGAAGACGACCTCGCCGAGATCGAGGCCGCGCGCGCCGCCGCCGCC GCGCACGCGTTGAAGGCGCTCCGGAACGCCGCCTCCTGCGCGTAGAGCGC GCGGGCCATCCCGACGCCTGCGCGCCCTGGCCCGGGAACGCGAAGACGG 30

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GGGCTGCTCGCCCACCGCTCGTCCGCGTCGACGGCGAGGCGCTCGATGC 10 CCGCGGGCCAGGCGATCGTCCCGTCGACCGCCGACTGCGTGAGGACGAGG CGGACCTCGGCGTGCTCCAGGAGGTGCCTGAGGCGCTCCTCGGGGAGGCG AGGGTCCAGGGGCAGGTAGGCGGCGCGCGCGCGCAGCACGCCGAGCACGC ${\tt CGGCCACCTGCTCCCAGCCCTTCTCCATGACCACGGCGACGAGCGCGTTC}$ 15 GCGGTCGCTCCGGAGCGCGAGGCCGCGCGGCGATCGCCTCGGCGCGCCG GGCGAGCTCCCCGTAGGTGAGGCGCCGCTCGGCGTCGACGACCGCGCACG CGTCGGGCTCCTCGACGGCGCGCTCAAAGAACGGCTCCTCCAGCCGGAGG 20 10 TGATCCGGGGTTGCGACCGCGGTGTCGTTCCACGCGACGAGGGCGCGCTC GCGGTCTTCCGGCGCGACGGAGAGCGCGCGGACGCGCTGCGGGGGTCCT GAGTGGCGCGAGAGCACGCTCTGCATCGTGGCGAGCATCCGGTCGATG GTCGCCGCGTCGAAGAGGTCGACGTTGTACTGGAGCGAGATCACGTCGCG 25 CCCGCCGCGCGCTCGACGCTGAAGCGCAGGTCGAAGCGCGTGGCCTCGA 15 CCGGGAGATCGAGCGCTCGATCCGCACCTCGCCGAGCTCGAGCGCCTCG GTTGGGGCGTTCTGCACGACGAGCATGACCTGGAACAGCGGCGAGCGGCT CAGGTCGCGGGGGGGTTGACCGCCTCGACCACCTTCTCGAACGGGGCGT 30 CCTGGTGCTCGAACGCCTCGAGCGCGACCTTCCGCGCCCGCGAGAGGAGC TCCTCGAAGGTCGCGCCGCCGAGGTCGAGGCGCATGACGATCGTGTT CACGAAGAAGCCGACGAGGGCTCGAGCTCGGGGCGAGGCCGGTTGGCGA 35 CCGCGGTCCCGATGGCGAGGTCGTCCTGGCCCGAGCTGCGCCGGAGGAGC ACGCCGAGGGCGGCGAGCAGGACCATGAAGCGGGTGGCGCCGCGGCTCCG GGCGAGCTCGTCGAGCTGCGCCACGAGGCGCGCGTCGAGCGGGAGGACCC GCTCCGCGCGGGAACGTCTGGACGGGCGGCCGCGGTCGATCGGTCTGG 40 25 GTCGGCGAGCCGCTTCCCCGCGAGGTGGCGGCGCTGCCACACCGCGAAAT 45 GCGCGCCGGTAGAGCTCCGCGAGATCGCGGACGAGGGGTTGGAAGGACCA GGCGTCCGTGACGATGTGGTGCGTGGACAGGACCAGGACGCAGACGTCGT 30

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CTCGTCCGGGGGCGTGCCGCGGAGGTCGACCACCTCCGCGGGGGCCGCCT 10 CGGGCTCGCAGATCTTCTGCGCCGGCGTGGGGCTCGCGACGAACACCGTG CGCAGGCTCCAGTGCCGCCGGACGAGCGCGGGGGGGCGCGGAGGACAGCGC GTCGACGTCGACGAGGTTCCGCAGGCGGACCGCCTGCACCACGTTGTAGG CGGTCCCGCGGGGAGCAGCTGCTCGAGGACCCACAGGCGCTCTTGCTCG 15 TACGAGAGCGGATACGGCTCGTCCGCCGGCGCGCGCCCAGCGAGGGCGC GATCTCGCTGGCGGGCACCGTCGCTGCGGCGGCGGTGGTCGAGGCGGCGC CGGAGGAGAGGCGATCGGCGAGCTGGTGGAGGGTTGGGTGCTCGAAGAGC 20 GTGCGGAGGTGCTGCGATGCCGAGGACTCGATGCGTCCGAGGAC <u>: 0</u> CTGCATGGCGAGCAGGGGGGGGGCCGAGGTCGAAGAAGCTGTCGTGTC GTCCGACGCGGTCGAGGTGGAGGACGGATTGCCAGATGTGCGCGAGCTCC 25 CGCAGGGAGGAGCTTCTTGTCGACCTTGCCCGAGAGGGACATGGGCAAGG CGGGGAGCAGGAGTGGGCGGCACCAAGGCGTCGGGCACCAGGCGG GCCATGCCCTCGCGCAGGTCGCGCTCGGAGGGCGGGTCGGCGCCCGGCAC GACATAGGCAATCAGGCGCGCGGGGGCGCTGCCTTGGCCGTGGAGGACGACGA 30 CGCCCTCGCGGACGGCGGCCAAGCGTCGCAGGGCGGATTCGACCTCGCCG AGCTCGACACGGCGACCGCGGAGCTTGACCTGCTCGTCGCGGCGTCCGGC GAAGGCGAGCTGTCCGTCGGGGCGCCAGCGCACCAGGTCGCCGGTGCGGT 35 AGAGGCGTGCGCGGGCTGGCCGAAGGGATCGGGCAGGAAGCGCTCTGCG GTCAGGTCCGTGCGTGTGTAGCCCTGGGCGAGGCACGCTCCGCCGATGTA CAGCTCGCCGAGGACGCCGGGCGGGACGGGCTGCATGTGCGGGTCGAGGA CGTAGACGAGGGCGCTGTCGATGGGTCGGCCGAGCGGGGGCTCGTCGCCG 40 25 GTACATGTTGAAGAGGCGGAAAGGGAGCGGTCGCCGGAGCGGATGGAGCT TGTCGCCGCCGACGGTCATCGCGCGCGAGGGCGATGCCGGTCCAGTCTTGC 45 TCGAAGCACGCCTCGGCCAGGGGCGTGGCCATGAACGAGAGCGTGGCCCG CTGAGCGACAAGCCAGGAGACGAGCGCTCTGTGGGAGAGCGGAGCGCGTCGT CGTCGGCGAGGAGGGGCGCGCGCGCGCGCGCGCGCGCCCAGATCTCG

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GTACAGCTCCCCAGCTCGCGAACGAGCAGCGCGAACGACCAGTAGTCGA 10 CCACGAGGTGGTGAACGACCACCGTGAGCAGCGGCGGCTGCCCCTCTCCG CGCCGCCAGACATGCACCCGGAGCAGCGGTCCGCGCTCCAGGTCGAACGC GCGGCGGCGCACCTCGTCCGCGCGGGGGGACGATCTCGCGCTCGTCCAGCG 15 CCATCGCCGGCTCTTCGGCCCATTCCAGGGCGACATGGCGGTGGACCTGC TGCAGCGGATGGCCGTCGCGCGTGAGGAACGTCGTGCGGAGCGCCTCGTG .CCGCTCGACGAGGCCCTCGAACGCGCGGCGAGCGCGGCCACGTCGACGC CGGCACCGAGCCGGACCGTCCTGCCCAGGTTGTAGAGCGCGCCGTCGGCC 20 GACTTCTGGCACTCCAGCCACATCGCCCGCTGCCCCTCGGTCAGCGCAAA 10 CGGCTCTTCCGGCGTCGCCACCCGCGGCGACGAGGGGCCGTCCGGACGG CCGGAGGAGAGATGACTGGCGAGCTGCGCGAGGGTTGGGTGCTCGAAGAG 25 CGTGCGGAGGTGCTGCGATGCCGAGGAGGACTCGATGCGTCCGAGGA 15 CGTCCGACGCGGTCGAGGTGGAGGACGGATTGCCAGATGTGGGCGAGCTC 30 GAGCTCGAGCTCGCCCGAGGGGGGCTCGTAGTCGGCGTGCGCGGGGG GCGCAGGGAGGAGCTTCTTGTCGACCTTGCCCGAGAGGGACATGGGCAAG 20 GGCCATGCCTTCGCGCAGGTCGCGCTCGGAGGGCGGTGGGCGTCTGGCA 35 CGACATGGGCAATCAGGTGCGCGGGGCGCTGCCTTGGCCGTGGAGGACGACG ATGCCCTCGCGGACGCCGGGCAAGCGTCGCAGGACGGATTCGACCTCGCC GAGCTCGACGCGGCGACCGCGGAGCTTGACCTGCTCGCGGCGCCCCCG CGAAGGCGAGCTGTCCGTCGGGGCGCCCAGCGCACCAGGTCGCCGGTGCGG 40 TAGAGGCGTGCCCGGGCTGGCCGAAGGGATCGGGCAGGAAGCGCTCTGC GGTCAGGTCCGTGCGTGTGTAGCCCTGGGCGAGGCACGCTCCGCCGATGT ACAGCTCGCCGAGGGCGCGGGCGGGCGGGCTGCATGTGCGGGTCGAGG 45 ACGTAGACGAGGGCGCTGTCGACGGGTCGGCCGAGCGGGGGCTCGGCGCC GAGGTCGGCGATCTCGGCGACCGTGGTGATGACGGTGGCCTCGGTGGGCC 30

TTGTCGCCGCGACGGTCATCGCGCGCAGGCCGGAGCCGGTCCAGTCTTG CTCGAAGCACGCCTCGGCCAGGGGGGTGGGCATGAATGAGAGTGTGGCCC . 10 GCTGAGCGACAAGCCATGAGACGAGCGCCGTGGGAGAGCGGAGCGCGTCG TCGTCGGCGAGGGGGGGGCGCCAGGCGAGCGGCGTCCAGATCTC GTAGACGGAGGCGTCGAAGCCGCTGGAGGCAACCTGAGTCCAGCGGTCGC 15 TGGGCGAGAGTCGAGTCGGAGGTGGAGGAGGAGGAGCCTTGAAAGG CTCGCATGGCGCACACAGACGCCCTTGGGGGTGCCGGTGGAGCCGGAGGT GAAGAGGACATAGGCCAGGTCGTCGGGCCTGGAGACGAGAGGAATGTGGG TGCTGGGCGCGCACGCCCCGTCCTGGACGAGGTGGACGGGGCAGGGGGCG 20 GCAGTCGGCGAGCATCTCGGCCAGGCGTGCCGGGGGGTTGGCGGGGTCGA GCGAGGCATAGGCGGCGCCTGCCTTGAGGACGGCGAGCTGGGCGGCGACC ATGCGGGGCGACGCTCGATGCAGACGCCGACGCCGCCGGGCCGAC 25 GCCGCGGTCGCCACCACAGGGCGAGCTCGGTGGACCAGGTGCTGAGCT 15 ${\tt GTGCGTAGGTGAAGCGCTGGTGGCCGAACTCGAGCGCGGTGGCGTCCGGC}$ TGTCGAGCGGCGTGGGCCTCGAACAGCGCGTGGACGCAGGCGGGGGCCGG 30 GGCGGAGGCGCCTGTCGTGCGGCGCGGCAGCGCCGCTCCAGTCGTCGAGGA GCAATGCGCGCTCGGCGTCGGAGAGCATCCGGAGCTCGGAGAGCGGTCGA CCGGGGTGCTCGACGGCGCTTTCGAGCAGGACCACGAAGTGGCGCGCCAT CCGCTCGATGGTGGCGGGTCGAAGAGCTGCTGGTCGTACTCGAAGCGCA 20 35 GGGCGATGCCGGCGTCGAGCTCTGCGGCGAACAAGGCGAGATCGAACTCG GCCGCTGCCTCGTCGGCGAGCGTGGTGAGCTCGAGCTCTCCCTGCGC GATCCGCACGTCCCCCACGCCGATCGCGAGGGCTGACAGGCGTGCATCCA ${\tt GCGATGGCGGGGTGCTCTGGAAGGCGAAGGCGACGTCGAACAGCGCGTCT}$ 40 25 CGCTGCGCCTCGCGCTCGCGCGAGCAGGTGCCGGAGGGCGCTGTC GCCGTGGGCCAGCGCGTCGAGGAACGCATCTCGCACGCGGGCGACGAGCG 45 GGGGACGCCCACGACAAGGTCGCTCTGTCCGCTGGCGCGATGGAGCAAGA 30 . CGGTGAGCGCCGACAGCAGGACCGAGAAGAGCGTGGTCCCGCGCTCGCGC

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GCGTGCCACGCCGTGTAGTCGCGCACGCAGAGGCTCGTGACGCCG GTCGACGGGGGACGGAAGCGCAGCACCACACACACACGGTGATGGC 10 GGCGTCGTCCTCGACGTTCACCACGTTGAGCGCGTCGCGCAGGACGCGCG GGCGCTTCATCAGCTCGACCAGGGCGTTGACGATCGCGCCGCCGCTGAGA TCCACGCAGCCCATGAGCAGCCCCAGGATCACGTCGCGGATCCCCTCGTC GCTCTCGTAGGTCTCGGGGACCGACTGCATGACCAGGTAGCGGTCCAGCA 15 CCGAGGGTTGCTCTGGCGGGGGGGCGACTTGGCCAGCTGCTTCTTCCGCGCG GCGACGATCGCGTCGATCATCGGCAGCGCCTCCTGACGAGCGGCCCTCGC CGCCGCCACGGCCGTCGGGTCGTTGGTCGGGTTGAGGAAGATCTCGTTGA 20 ACAGCGCGTGGGTCCACGCCACCTTCTCGGTCGGGATCTCGCCGACG CCGAGGTACCGGGCCATCGCGCCGGCCGGCACCCTGAGCGCGTAGTCACC GGTGAGATCGAACGGCTTGTCGACGCCGACCTTGGCGAGCAGCCGGTTCG 25 GCGAGGCGCAGGAGCGACTTCTCGTGCTCGTACTTGGGCGAGTCGTTCAT $\tt CGCCAGGATGTTCTGGCCCACGTTCTCGACCAGCTTGGGCGCGATGTTGT$ 15 CGACCGAGAAGACGTCGTTGGCGTTGAGGACCTCGACGACGTCGTTGTAC 30 CGGGTCACGAGCGTGATGGCCGGGATGGAGAAGATGGGCTTCTCGCGCCG CAGCTGGCTGAGGAACGGGAGCGGCTCCTCCCTCAGCCACTTGAACACCA TGCCGGCCTCGATCTGCTTCCGCTTGACCGGATCGTTCTCGTGCGCCAGC GCGCTGTGGAGGGCCTGCAGGTAATCGAACGGCGGCGCCTTGGCAGCGTC 20 35 ${\tt CGCTCGTCCTTCTTCGATGTGAATGCTCATGGGGAGAATTCCTTTCT}$ ${\tt CGCATGCCGATCAGATCGCGACGCTCTGGGGGACCATCGACGGGAGCAGG}$ TACAGGTACGGCTGCTCGCGGGCGCGGTTGCGCTCGGTGATCTCCCGCTC GATGTGCGCCAGGCGCTCGCGGTAGCGAGCAAACGCCTGCTTCGCCGCCG 40 GATCTTGCAACAGGCACTTCATCGTCATCAGGCTCTCGCTGGTCAGCGGC GGGCCCATGCTGAGCGAGCGGCTGAGCACCATCTGGCGGATGCTCTGCGC GCGCCCCGGGAGGCGCTCCAGCGGCTTGAACTGCCGCTTCTCGCTTCCGT 45 TCAGGACATCGCCGTAGGAGCGGTAGGTGGCAAACTGAGCGTTCGGGATC CAGGTGTAATAGTCCGTCTGCCCGAAGTTCACGGCGGCGTGATATGCGGT CGCCGTGAAGATGATGTTGGTGACGATCGCGATCAGGTCGTCGAGGCTCG

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TGAGCTTCTCGAGCTGATCGGCTCGCTCCGGCGGGAGGAGGCTATCCATG CCGCCGAGCTGGGGGGACACGAGCTCGTGGATCCACCGCTGCAGGCTGGC GTCGCTCGACAGAGACCCCGGCGTCGGGTAGGCGATCTTCAGCACCTGTC CGACGTACTCCTGGATCGCGTCCCAGTGCAGCAGCGCGTCGTCGCGGTAG TGATAGCCGACCAGGTCGCGGACGTCGCGCGCGACAGGTCGCGGGGAG CGCGCTCTCGTAGAACCGCCACGGCTTGCCGCCGTACCCTTTGATGCCCT TGCCGGTGTAGGCGCGCGTCAAGAGCTCGAACGAGCCCATGGTGGCCACC GAGCTCGTGATGTCGAAGAAGCGCCCTCGCCCGAGGAAGCGCCGGCGAGC CAGCTCGTTGATGGCCAGGGTGTTGAAGAAATGCGGCCTGAGCAGCTGGT GGAGCGGATGCGTCGCGGGCAGGTTGCGGTAGGTGCTCACCGCGAACGGC TCCACGATCAGGTGCGCGTACAGCAGGTGGGTCACCTGGCCCTGGTAGAT GGCGTCGGCGCCGACGGCGATCTTCGCCGTGAGCCAGTCGTCCGACG GACCCGAAGGGGTGAAGATCTTGTCGGGATGCGCCCCTTTCCCGGGGCGC GAGTGCACCAGCCTGATGGCCACGGGCAAGAGCTCACCGGCCGCGGTCTG GTGCAGCATGCACGTCGGCGCGCGGGTACTTGCCCAGCTCTTCCTGCA CGTCGGTGTCGACGATGTCCTTGAAGATGCGGTAGTCGAGGAAGTAGAGC TGCCCGCCCTCGCGCACCTCCTCCAGCGTGCGACCGTCGGCGATCGCGAT CGGCTTGGGCTCGGCGCCGCTCACGAAATCGGCGAGATCGGCCGGGGTCG CGCGCCGGATGTGCCCCGGGTTGATCCCCACGAGGCGCTGCCGCCCGAAC TCGGCGTCCTCGGCCCAGCGCGTCGCCACGAGGGGCTTGCGGATGAAGGT CCACGGCTTGAAGAACTCCTCGAACTGATCGAAGCTCTCCCAGTTGTCGA TGGACTCGAAGATGGCGCCCAGCCCGAGGTCGGACGTGGCCCTGAGGACG AACTTCCCCTCGCGATAGCGCTTGTACCCGTACTCGAACAGGTGAAGCGC CTGCGCGATTTGCAGTCCGGCAGTGTCCTTCCACTTGCCGAGGTTGAGCG CCAAGATCTTCTTGATCGGAAAGCCTTCCCCCGGCGGTACGGAATCGCTG CCCGCCGGCAGGTTGGACCCGAAATTGCGCCAGTTCGGTGTCGAGCTGGG CGGAATGGTTCCGTCTCAGTCGCAACAGGACTCAGTACATCCAGCGCCGC

CCCCCGTCCTCGACCTGCCCCCGCAGCCGATCGCGCCCCTTCATCGTG

ACCGATGCTCACGCGTGCATTGTTGAGGCTGCTAGAAAACCGTGGAGCGT . 10 TCACGCATGTCAAGCCATTTTGTTCGGCGCCGCGGCGAGCGGCCGGATGC CGCGCGCCCCGCGCGGGGGTGTTCGCTCCCGACGTACCGCTACCTCGA CGACGTATGGCTTGAAGGGCAACCGCGCAAGTCGTCCGATTCGTGCTCGT ATCCTGCTCCTTCCAGCAGGATTTCCCCGCCGCCAGCGGCACAAAGGTGC 15 CAGGGCGAGCAGAAAGAGCGCTGCCCGCCCCTCCCCGGCCGCGCTCGCCT .TTAGTTAGCCTAGCTAACTTCAACACTGATGCGACTGATCGGGCCGACGC 20 AACCGACGCAACCGACGCAACCGACGCGACCGACGCAATCG 10 ACGCAACCGACGTGACGGACGCTGGCGACTCGAAGAAAACCACGGACGCA CTCCACGTCATCGACGTCATCGATGCGCTCGATGCAATCCA TGCACTTGACGCGATCGGTGCGAGCGAGGCGACGAGGTCCTCTCGTGAAAC 25 ACCGAACCGAGTGCCGGTAGCGGGCGCGCGCAGTGTATGCTAGGCTCGG 15 $\verb|CCCTCTTGTCGAGGCCGCGCGCTCGGCGTCGAGCGTGGGCTCGGGTGCC| \\$ CGCGACGATCTACAAGGTGGTGGTGAACCACGAGGAGCAATACTCCATCT 30 GGCCGGCGGACCGAGAGACCCGCTCGGCTGGACGGAGGCCGGCAAGACG 20 GCGCCCGCTCAGCCTCCGGAAGAAGATGGCCGAGAGCCCCTGAATCGCGG 35 CCCGCCCGAGCGCCGTCGCGAGCGGCCGGGCGGGCTCAGCCGTGTC ATCGTCGCGCTCGACCGGCCGCGCGCGGGATCGCGCGAGCCCGGCGG GGTCGTGCGCGCGGCGCTTGTGCCGGGGCCCCCGCTCTCGTACGCCTCC GTCATGCCGCCCTCGATCTGCACGTCGCCTTGTTCGGCGCCTCCGGCGC 40 25 CGGCAAGACGGTCCTCCTGGCAGCCTTCTACCGGGCGCAGACCCAGCCCT CGTTCCAGCAGGAGTACGCGTACAAGATCCAGGCGGTCAACAAGGCGCAG GGCAACCAGCTCCTCGGCCGGTTCTATCGCCTCGAAGAGGGCAGATTCCC 45 GGACGGCAGCACGCGCTTCGACGAGTACGAGTTCGACTTCTTCCCGAGAG ATCTGCCCGAGCCGGCGGTCCGCATCCACTGGTACGACTACCCGGGACGC TGGTGGGAGGCGAGCCGGTCGACGCGGACGAGCGGAGGCGATGCGCCA

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GGGCCTCATCCGGCTCGGGATGAGCCAGGTGGGCATCCTCCTCGCGGACG GCGCGAAGTACCGGGCCGAGGGCACCGGGTACATCCGGTGGCTGTTCGAG 10 CACTTCGCCGACGAGTGCGACCGGCTGCGCCGGGCCAGCGCCACGGG CGACGAGGTGAGCTTCCCGCGGGGAGTGGATCCTCGCCCTCAGCAAGGCCG ATCTCTGCCCGCCGGACTACAGCGCGCGGGACTTCGAGCGCGAGGTCTGC CGGGACGCCGACGATCAGCTGGCGAAGCTCTGCTCGGTGCTCCGCGCCGA 15 GCACGCGTTCGGCCACCGCTTCATGCTGCTCGTCGGTCGCCCCCGG CCGGCGCGCAGGTCGATCCGAGGACCTCGCTCGGCGTGCGCACCCTCGCC CCCGCGATCCTGGTGAGCACGGTCGAGGGCGCGGTGCGCGAGGCGCAGGC 20 10 GGCGAGAAAGGAGAAGTCGGCCGGAGAGACGTTCTTCCAGGGGCTGCGCG ATCTCGTGCAGTTCGTCGACTCCCTCGACGACTTCCTGCCGAAGCGATAC CAGATCGTGAGCAAGATCCTGCGGTTCATCTCGATCAAGGACTTCGCGAC CACCCGGCTCGACCGGCTCAAGAAGATGCGCGAGGACGCGATCCGGAAGG 25 GCGACACCTTCACGGCGGTCCTGACCGCGATGGTCGCGGCCCTGCGCGAC GACGAGGGCGCCCGCGCCTACCACCAGAACCAGTGAGGTCGTCATGCCCG CGCCAGCGCCCTCGTCGAGACATCGCGCCTCCTCTGGAGGACGCGCGGC 30 GAGCACTGGGATTACGAGTTCATCTGTGTCCCCGAGATCCCGGCGCTGCC CGCCTGGCTCCGACGCTCGAGGCGATGCTCGCCGACGCCGACGCCGGCG CCGGGGAGCTCCGCTATGGCCTGCTCGAGATCGACGATCGCGGGCAGAGG GCGCCGCGCCTATCCCTACGTGGCCGTGAGGTTCCTCGATCCGGCGCG 20 35 GAGGGACTGGACCGGACGGCAGGTCCAGCACTTCGCGGCCTGGTTCCCGC CGGTCCCGCCGAGGCGGTCGCGGAGTTGCCAGAAGCGGTCCCCGCCGAC TGGCACCTTCGCGTGCTCGACGGGCTCGCGGGGACGTACGGCTCCGGCGA GGTGTTCGGGCTCCCCGAGGCGACGATCCGCGCCTGGAAGCGGAGCCACG 40 25 ACGAGAGCCGGGCGCGCGCGATGGCGATCGTCAAGGCGACGCCGCCG GTTTCGCTGGGCGGCGAGGCGGCGCGCGTCGCGGTGGACGCGGGTGCC 45 CGGTGGGCGGCCTAGCGGCCAGGGCCGATTCGCCTGCTTCGCG ATCGGCGCCATGATGCTCGCCGCCTTCTGTCGACTGATGCTCGCTTGCGG TGTGCGCCTCCTCGGCGCCTGACGGCTGCGCCGCGCGCAGGCCATCCGACGG

GGGGTCGCCCGGCCAGCGCCCGCCGGGCGACACCAGGGCATCGGCCCTC CGCTCGGGGCATCGATTGAGCTCTCCGAGCGGCGGTCCGTCGATCGC 10 CGCAGAGCTCCCACCGGGCGGAGCAGCTCTGGCCGGTGACCGCATAGGGG TTCGTCGGGCAGGTCCACCACTCGCCCTGGAAAGGACGCGGGTTGCAGTG CGGGAGGCACTCCACCCACCCGACGAGCACGAGTTCCCTACCGAGACGG TCGGCTGAGCCGCGCAGAACCAGCGTTTTCCTGCGAACCAGCCGGGATTG 15 CACACATCGGGCGCCCGCCGACGGGGGGGATACACCGTGGCGACCGCCTG GATGTCCACGGCGTCGAGGGTCTCGCTCCCGAAGCGCACGCCGTCCTGAT CCGAACACCCACTCCAGTAGGTCATGATGGAGTCGTAGTAGAAACCA 20 10 GGGTTCACGACGATGTACCGCCGGCTCGAGGGCCACCCGCTGGCGACGTC GCTCGCGGGGAGCGGCTCTCGTTGGCTGCAGGCGCTCGGGACCAACGGGT GATGCCACTCATGCATGAAGCCGATCGCATGACCCATCTCGTGGATCGCG TACTGCTCCACGCAGTCGAAGCTGTATTCGACCCGGGCTGTCTGCCAGTT 25 GTACTTGATGCAACGGTTGAAGTCGGCGCCCCAGGGCTTGAACTGGACCG 15 GGGTGGATCCTGACGCCGACGTAGGTCATGCGAGTGGCCGGCAGGAGCGA ATCGCAGCTCTCCCAGCCGGTGAAGCGAACCGAGCTCCAGCGTTCCCAGC 30 TTGGGCGCATGGATCAGCCCGCCGCGCGCGCGCCGTCGACCCTCTGCTCCGC CGAGCTCGTGGGGTCGATGCAGACCGGGATCCGGACATGGCCGTCAGCGT 35 CCTCAGGCCAGCGACTCGCGCTGTCGAAGACGCTCGCCTCGGCGGACCGC GGCGCGGGGGAGACGGTCAGCGCGCGCGCCCAGCGCTGCGAGGAGCAGCGG ACCGAGCGAAGCGGAAACCGCACATGTCGTTCAGGGCCCCGCGTCGTGC GGTGCACCGAGACAATCTCGAGCGGGCTCATGGACGCAAACGCGTTGCGA 40 25 TGGCCTTGCAGCATGTTCTTCTCCAATCGACGAGGGTTGTTCTGCTGAAC GCGGCTCCAGCGTGGAGCTCGACGCGGTTCACCGGCTTCACGCCGGGGCC GTGGACGAGACCCGAGCAGGGGGGGGGGGGGGGCGCACCGGCTCGCGGC 45 GCCTCCACCCTGCACCTACGACGAGCCTGCCGCTCGGTTTCGCGGAAAAT GCCACCCGCTGCCCAGCGGGCGAAGCGCGGACGAGGCGCTCGTCCCCAC GGTAGCGCCGGTGCCGCTCCATCGCTCCATGGGTCGCTGCC

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 $\tt CGCGGGTCGTCGAGGAGACGGACCCGGGGCGCGGATCCCTGGCTCGGCGT$ CGCATAGCTCGTAGGGGGGGCCTTGAGCCGGCGGTACGAGCGGCGCAGTT 10 CAGCAGCCGACCACGTGGACGCGCGCGCGCTCCGAGCTGCGCCGAGGAACC CTTCAAATATTCAGATGGAATTCACAGGGTGGCTGAGAGACGGGGAGTAA GATCTCAGAGATCTCCCTGCCTACCCGCATCCCTGTTCAATTTTCCGCCC ACAACGCGAACGGATGAGGAAATATCAGCCCGCGATCCCGACGGCCGACA 15 GCATCAAAGGCCGCTCGAATCCAGGGGATTCGAGCGGCCTCGGTCGCGCG GACCCCCGCCGCGAGCCGCTTTGTCACCACTTCACCACTTCAGAGCTTCG ATCATCTTCTCACCATAACGCGTGCCCATGATAACAACGGACGCATGATC 20 CCATAGGCAGCATGTCGGCCGCTTGGTGCACGAGGTTGTTATGACCGCCG CAGCACCCGCCGCGGGGAGCTCTCCGAGAATGAAGGGAACGTCGTAGTC GACCCCCAGGCTGCTTTCACCTCGTTATAGAGCTGAACGACCTTGCCGG 25 GCCACGAGCTCTGGCCGTTGTCGGACTCACCCTGGTGGAAGATGATGCCC 15 GCGAAGCGCGCTTCTCGGCCGTCTTCGCTTTGGCGATCTTGTTCAAGAT CATCTGGTGATGCGAGCCACCAGTGATGAACGTGTTGATCGACTCGCCGC TCTCAGCGGTAGCGACCAACCCGATCGTATCCCCCTCAGGCAGCTTTCCG 30 AGCAGGGTCTTGCCGAACCAGATGCCCGGGTCGACGGGGTCGACAGGTT CCATCCTTTTCACCAGGGCAATCGCTGAGCGGCGGATTGGCCAAGTTCC ACTGTCCGGCCGGCTGATTGCATCCGCCGAGGACCTTGAGCCGCGCGTCA 20 35 GAATTTTTGTCGCTGTCCTGTTTGTCTGCGACACCAGCCATATTCGACTG GCCCATGAGCATGAAGATGTGAAACGTCGGACTCGCGCTCGGTGCGCCGC CGGTGCCTGCCGCTGCTAACGGATCCGGTCCCTCCCGTGGCGTCACCT CCAGTTCCAGCGTTCGTGCTGCCTGTCGCGTCCCCGGGCCT 40 25 TGGCGCCGGTCCCCGAGCCGGCCCCTCCGGTGTTGTCGTCCTCACCG GTCGCGCCGGACTCGCCACAACCGGACGCAGCGATGATGAAGAGGAATGG 45 GAGGAGCAGGAACCTGGGTGTGCCTCGGGTCGTGCGGTTCATCTCGGTCA TGATCGTTACCTCGTCGCGCGGGGCGCGATCTGAAGAGCATGGCGGAAT CGGTAGGCCGGCGTCGCGATGCCGGCGCGCGAACCTCGCCCGCAAAGAG

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 ${\tt CTCAGCGCCGGGGCCTACCTTATCGCATCTTGGGCGCTCCAGGA}$ TTCGGCCTTAGACAGCACAAGCAGAAGACCTTTGACACTGGATTTTTTCA 10 TCGAAGCGAAGCGGTTTCACGATCCGGGATCGCGGAAATTTGAAACGGAC GCGTCGCGCGGCAACGCAGGGGACTCATCACGAGGCAACCGCGCTGCGT CGCGAAATTGGCCAGCCTCTCGGAGTCCCTAGTTCCGTGCGTCAGACGCG 15 TCACCCACCATGTCGAGCTCGGCGCGCGCGCTCTACGTGCTTGAAAGACCT CCGCGAGCGCCGCTCTGCGCTCCGCGAGCGCACCAGGCTCCCCGTGGA TTCAGGGCAAGGCGGTCGTGATCACGTCCTTCGTGGTCGCCGTGCTCTGG 20 10 CCGGGGCGGTCGACGCAGGACGGGTAGTACTGGCCGGCCCCGTTGAGCTT CTGGCAGACCCGGTCGCACGACCCGGCGATGCGGATCAGCCCGCACTCCA CGATCTGACCCCGGAGGTCACGTGGCCCGCGGCGCAGTCGCGCTGGTAG GCGCGCGAGTTGTCGACCGTCGCGCTGTTGTAGCAAGCGTTGATATAGGG 25 TTGCGCGGCGAACAGGTTGCCCCAGAAGGCCCCCTCGACGTCCGGATAAT 15 CGATGAGCTCCTGGCTGGAGGAGAGCGTCTTCAGCGGATCCCGCAGCGAG CGGGGGGAGAGGAGCACCGGTACTTGATAGTAGTTCACGCGCGCCGCCAC 30 GCAGCTGGACACGATGCGCTGCCTGCGTCGTCGAGCGGCCCGCTCGCCC ACGCGGGCGCGACCCGAGCAGCCCGGGGTAGCGCTCGTCGTGCCTCTTG $\tt CCGTTCGAGTCCGTCCACGAAAAATCGAAGGAGGCCGTGCTGCTCAGGGC$ 20 35 CGGGATCCTGGATCGCGGCGAGGTTCCGCGCGCTGAGGCCGCTCAGGTTC AGGGCGTTCAGGTTCAGGCCTTGAGGTTCAGGGC GTTCGTGCTGAGCGCGTTGCCGCCCACGAGGGCCCCCTGGGATTCCCCCA 40 25 AGCACCCCTGCCCAACCAAGCACGATGAATGTCCGCTCGAGAGACATGGA CGCGGGCTCCCATCGATTCGCTGGATGGGTTCAATATTCTACTTTTTCCC GCGCTCTCGCGCCGGTGAAAGTCGCTTCAGCGGCGGCGAGGTCGATGTCA GGAGCGTCCGACTCCGTCGCTCAGCTCCGCGTACCAGCGACGGAG 30 TCGCCCGCCCATGACGGTCGGAATGGTAGAGGCGGCCGCGAGGGCCGCCT

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10 GGAGCGCTCCTCGAGCGCGGCCCACGCGGCGGCGGTCGTCGCGGGTCG CGAGCTCGATCATCGCGCAGAGCACGTCCTCCGAGGGCTTCAGCGCCTCG GCCCGCCTCGTCGCCCTGGTAGAGGCGCAGGCGCGCGATCAGGAGCGTTA 15 CGACGACCGGCGCGTGGCGATCGCCGCAGCGCGCGCTATCGCCTGGACG GCGCGCGCATGGGGCCTCGCGGCCCCCGAGATCGTCCATCAGGTACAGGTA CTCGGCGAGGTTGTAGCGGCCGACGAGCTCGAACGCGGGCTGGCCGAGCT 20 CGCGCCCGAGCGCGATGGTGCGCTCGAAATCGGCGATCATCCCGGCGCGA GTGCATGAGATCGCTGCGCTCCTCGCAGCTGAGGATCACCGCGTCGAGGT CTCGCGCCCCCCCCGACGCCGACGCCGACGCCAGGATGAAGCCGAGC 25 AGCAGCAGGGCGATGATGTGCGTCTCGTGGCCCTCGTCCCCGAGCCGCGC 15 CGCCTGCGCGCGCGCGCGTCAGCACCGCGGCGCCTCGTCCTCGCGGT 30 AGGGGCGAGGCCACCCGGCCGAGGCGCTCGGCGGCCGCGACCCGCTC GCGCGCGCCCGTACTCGCCCGTCCAGTCGAGGATCATGGCCTCGTCGA CGCGCCGCGGGGGCGGGGCCGAGCCGGAA 20 35 GCGCCTCGACGCCCCGTAGCAGCCCTCGGCGTCGAGGTAGGCCCGGCGC CAGGCCGCCGCGCAGTGCGCCGCGAGCACCAGCGGATCGGCCTCGC 40 25 CCGCGGCCTCGAGCCAGTCGGCGGCGAGCGCGCGATCG CGGGATCCTGGATCGCGGCGAGGTTCCGCGCGCTGAGGCCGCTCAGGTTC 45 AGGGCGTTCAGGTTCAGGGCGTTGAGGTTCAAGGCGTTGAGGTTCAGGGC GTTCGTGCTGAGCGCGTTGCCGCCCACGAGGGCCCCCTGGGATTCCCCCA 30

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AGCACCCCTGCCCAACCAAGCACGATGAATGTCCGCTCGAGAGACATGGA 10 CGCGGGCTCCCATCGATTCGCTGGATGGGTTCAATATTCTACTTTTTCCC GCGCTCTCGCGCCGGTGAAAGTCGCTTCAGCGGCGGCGAGGTCGATGTCA GGAGCGTCCGACTCCGTCGCTCAGCTCCGCGTACCAGCGACGGAG TCGCCCGCCCATGACGGTCGGAATGGTAGAGGCCGCCGCGAGGGCGCGCT 15 GGAGCGCTCCTCGAGCGCGGCCCACGCGGCGCGGTCGTCGTCGCGGGTCG 20 10 CGAGCTCGATCATCGCGCAGAGCACGTCCTCCGAGGGCTTCAGCGCCTCG CAGCCGGCGTCGTCTCGCGCGCGCGCGAGCCGCAGCGCGATCCGGCGAGC GCCCGCCTCGTCGCCCTGGTAGAGGCGCAGGCGCGCGATCAGGAGCGTTA CGACGACCGCGCGCGCGCGCGCGCGCGCGCTATCGCCTGGACG 25 GCGCGCGCATGGGGCCTCGCGGCCGCGAGATCGTCCATCAGGTACAGGTA CTCGGCGAGGTTGTAGCGGCCGACGAGCTCGAACGCGGGCTGGCCGAGCT CGCGCCCGAGCGCGATGGTGCGCTCGAAATCGGCGATCATCCCGGCGCGCA 30 GTGCATGAGATCGCTGCGCTCCTCGCAGCTGAGGATCACCGCGTCGAGGT CTCGCGCCGCCTCCTCGACGCGGCCGAGGCTGGCCAGGATGAAGCCGAGC AGCAGCAGGGCGATGATGTGCGTCTCGTGGCCCTCGTCCCCGAGCCGCGC 20 35 CGCCTGCGCCGCGCGCGCGCGCGCGCGCGCCTCGTCCTCGCGGT CGGCGCGGTGGAGCGAGCGCCCACGCCGAGGAGCAGGCGGCGCCGAGC AGGGGCGAGGCCACCCGGCCGGCGAGGCGCTCGGCGGCCGCGACCCGCTC GCGCGCGGCCCGGTACTCGCCCGTCCAGTCGAGGATCATGGCCTCGTCGA 40 25 CGCGCCGCGGGGGCCGAGGCCGGAGCCGGAA GCGAGCGAGCCCCGCGCTCGGCGCTCCTCGGGGAGCAGCGCCGCCGAGCA 45 GCGCCTCGACGCCCCGTAGCAGCCCTCGGCGTCGAGGTAGGCCCGGCGC CAGGCCGCCGCGCAGTGCGCCGCGAGCACCAGCGGATCGGCCTCGC

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CCGCGGCCTCGAGCCAGTCGGCGGCGAGGCGGTGGCCGAGCGCGCGATCG
TCCTTGGTGAGCTGCGCGTAAGCGCCCTCGCGCAGAGCGCCCTGGCGGAA
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TCGCCCCCGAGCAGGTGCGCGACGGCGCCTCGCCAGAACACCTCGCCGAG
CACGCTGGCGGCCCGCAGGATCCGGCGGCGCGGGGGGGCGCCTCCA
GCCGGACCTGCACCATCGCCACCGTCTCGGGCAGCGCTCGCCGGG
CCCTCCGCCGTCGCGGGATCAGCTCCTCGAGGAAGAACGGCTGGCCTC
GGACTGGGTGACCAGACGATCGATGAGGGCCCCGTCGCCGCG
GGACTGGGTGACCAGACGATCGATGAGGGCCCCGTCGGCCGCCCCA
GCGCCTCCCGCGGGAGCTGCCCCACGCCCTCGGCGGGAGCTGCCCCA

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© GCGCCTCCCGCGCGAGCTGCGCGCACGCCCTCGGCGGGAGCTGCCTGAG CAGAGCTCCTGCCGCCCGCGCCCAGAGATCGGGGTACGCTTGC,

or their complementary strands,

15 (b) DNA-sequences which hybridise under stringent conditions to regions of DNA-sequences according to (a) encoding proteins or to fragments of said DNA-sequences,

(c) DNA-sequences which hybridise to the DNA-sequences accord20 ing to (a) and (b) because of a degeneration of the genetic
code,

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(d) allele variations and mutants resulting by substitution, insertion or deletion of nucleotides or inversion of nucleotide segments of DNA-sequences according to (a) to (c), wherein the variations and mutants offer isofunctional expression products.

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13. Peptide encoded by a DNA sequence according to claim 12 selected from the group consisting of

PCT/US99/23535

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WO 00/22139

Seq ID No 92 10 >Contig11_002 591 amino acids MW=63639 D pI=5.80 numambig=0 MLDVWSTSDQVACRLHCAGAGPSASLELRYDASAGARRDAERLAERLAALLEDLSRHPER PVAQGEYVGPGERAEIEAWSRGPAMELPSACALHRWFEERAEQHPDVVAVRSEGKSLTYG ELERRANRLASCLRRRGVGLDTIVGVCVPRSEDMVVATLAVLKVGGAYLPLDHEYPGERL 15 AFMMRDARARLLVTHDAIADELPTGGWTTLLLDAEAAEIAACSDARPAVSPPPDSGAYVI YTSGSTGTPKGSLISHRAIVNQMQWIQRYWALTADDRVLLKAAFGFDVSVWEIFWPLSFG ARIVVARAGGHRDPEYLRRLVRDEGATTAYFVSSMLAAFLGGPEQPFPASLRKVLVGGEA 20 10 VPLDLVRRFYAKHDGDLINMYGPSEAAIAVTGCVLPSDPRVTWVPLGAPVANAEVFVLDG ${\tt AMRRPAIGALGDLYIAGAPLARGYVGQPGLTAERFLPDPCARAAGGRMYRTGDVARFLPD}$ GMLEFQGRSDHQIKLRGHRIELGDVEAQIRRVPGVGQAAVVLREDAPGDARLVAYVVLDG DAAGDAPDVRAGLKASLSAYMIPSSVVRLYALPMCSERLAFTGSSYAGCLL* 25

> 15 Seq ID No 93 >Contig11_007 361 amino acids MW=38862 D pI=10.42 numambig=0 MSDHEMTGFSLSPQQRAIRALDREAGAPGCRTLAVVAVTGPCDEGRLSAAALALAERHEI LRTRLVEAGRARPRRWSASRASRGRQQDDWVGCSEAEQGERMSRLVARLSEDRGADDGLR VGLVRVGPEERRLVLAAPAWCVDEESIAPLVRELCASTAGAGAPPEQQYADVAEWLNGML ESEDAGDGRRFWAERRSHFGPPLHLAFSRGGAGAGSGRARVDLGQGGMAQVERWSSSW 20 QVPQRIVLLALWASLLWRMSGGNEPEVTVAVRFDGRSLDALAGAVGPFARFLPVRIEISA SDTLADVARRLALAEAEAAAHQDAAPGVSHRMSWGLLRRGGRAGAVARRRAGPRARRLEH ٧×

> 25 Seq ID No 94 >Contig11_012 882 amino acids MW=95015 D pI=12.69 numambig=0 MARALYAQEAAFRSAFNACAAAARARGLDLGEVVFREGEGDGRTLLGTALAQPALFAVEL ALARLWMSWGIEPAAMIGHSLGELVAACVAGVFTLEDAMSLVIDRGRFMQAAPAGSMLAV GLPAADVEGLLEAGLEIAAVNSPKITVVAGPASAIRDLAARLEAREVFARPLQTSHAFHC ALIDGAVAPFLESVRRARLSPPEIPVVSNVTGALLTDAEATDPAYWARHLRQPVRFSDGV 30

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EALFASGHALFLEVGPGRGLTTLVRQTLAGRGGAAIASLGSTHAASEPASLAEALGQLWE
AGHAVDWTARPRGRPPARSSACRRTRSSGRGTGSRRAAAPPPPSRRRPTRPSRPRRTPSR
RRRSPARTPGPRSPRRRPSPSARSPAIWERPPRRPRDRRPRRLLRPARRLARRDPGDVPD
PRAARRAPAAGALPGADGRGARGPGRRAPRGAAARVPPDRADPPRRPAPAVVRAAPA
VVRRSARAGQPGVQHPVRGARDGPARRRRAPPQPVRDRAAPRGAADDVQRQGRRAVPGRR
ARGPGAVPDVRPRAPRGRGPRRGGLGARPRGEPRAVRPEPRAAPPRAGHPEAPRRARHRA
RRAPRRVRRLVGRRLRRRARRALRLRAGPAFPAAGAPGAVRRLRRSPAGVAVRRGPGGR
APVLDDEALGRAAPGPRAGRPRAGGAKDVARGAAEPRRGRAHPPDQGVLRAGGDLPLHG
PARRVQARPAPAHRARGPRRGHRRREPEPRRDRADDRLLRQPARAPDRLRGRPDVRRAGP
PRARRRARGVRAPGPAVRPARRGPAAEGGRRARAPLRREVRHAQRARPPDEARGARARGA
GGRGDHDGVRLRPHGRRGRRLVPLRRRAQQRAVFGGDGRQFP*

>Contig11_021 1213 amino acids MW=131017 D pI=12.40 numambig=0 MRGRRRRAAPHLRGARPARRGDRRGGLALRSDRERARRRGHGEGLGAGGRRARRAARRRR ${\tt LPAPGPSPPRGAPQAPPGARRGPPRPHAVGGRRDDRLARGHRAPRRRRGRAVARAARRAP}$ ${\tt AARRKHGRPGLRDLHVRVHGAAQGRDDRPPRRGEHGPRHQPPLRRRPGGPGARALVAELR}$ PVGLRRVRDARRRRRRDPRPYPRLGSGALARARGARAGDRVELGPGADGDAHGRVPRRG RPGAVVAPPRHDERRLDPAEAPRSHPRGLPRAPRREPRRDRGVDLVDRPPDRGRRPGVA QHPLRPPAREPAHLRARRGAGAVSDRGPRRDPHRRDRRRARILARRGADPGAVPEAPHDR RAAVQDRRPGPLLRRRDHRAARAHRPSGEDPRLPHRARRDRGRPRAAPLGRAGGRGGEDRSVGREAPGRVRRRRRRWRRAPRLRPEEAAGVHDPRGGRRPPGAAAERERQGGPRRPAGS RRGRAARRGRRPADRDRAAHRLGARGGLAGRGRRRDRQPLRARLHLAAPRARAAPARRAH ${\tt RGARARRGRRGAGRVADRPVPVPDHRATGAAARRGDGQGRAGRRRGAARRGAPRRATPPG}$ ARIAMSEPIETEDGGSDIAIVGMAGRFPGAPSVDALWENVRRGVESIARFPESEREEPPV GASAAPGAPVVCAGGLLDDIDRFDASYFGYSPREAQLMDPQQRLFLECAVAALEDAGCDP ARFPGAIGVFGGCGSNTYLLQLLSHPDLAATVDPHALMLASEKDYLATRVSYKLDLHGPS VVVQTACSTSLVAVHMACESLLGGQCDLALAGGVSIGIPQKRGYPYVPGSICSPDGRCRP FDARAEGTVGGSGVGIVALKRLADALRDRNTVHAVIRGSAVNNDGGRKVGFMAPSVDGQA

AAISEAQSVAGVDPGSIGYVEAHGTATAIGDPIEVEALTQAFRRKTPRKAYCALGSIKAN

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Seq ID No 95

IGHLDAAAGVAGLIKAAHVVRSGEIPPCVHFEAPNPKLDLAASPFFVPREAAPWPRELRP RRAGVSSFGIGGTNAHVVLEEPPPLPPRAPAPERDHVLTLSARTPEALSTACAQLAAHLE ATDVPLDDVAFTLQTGRAEHPYRRAVVARTRAEAIQGLAREGASALARPDEPRPSSRSRA RARRPSGWPARSTRRRRRSGAPSTRARRRRGRAASISARSSSARARATGARCSAPRWRSP RSSPSSSRSPGSG*

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Seg ID No 96 >Contig11_026 3079 amino acids MW=332984 D pI=5.97 numambig=0 MLTVVDHHVVVEYWSFALIVRELGELYSALRAGRPPQLPPPSSFFAAGVSCPSPREAAGG AEYWRKALDGATTAIDLPRDRARHDAGARRGRAHAITLPKPLTGALARLARERGTTLFSV $\verb|LLSALTVLLHRASGQSDLVVGVPSAGRHDDESARAFGYFVQMLPVRVALRGAASFDALVA|$ RVRDAFLDALAHGDSALRHLLARAQGEAQRDALFDVAFAFQSTPPSLDARLSALAIGVGD VRIAQGELELTTLADEQAAAEFDLALFAAELDAGIALRFEYDQQLFDPATIERMARHFVV LLESAVEHPGRPLSELRMLSDAERALLLDDWSGAAAARQAASAPAPACVHALFEAHAARQ PDATALEFGHQRFTYAQLSTWSTELALWLRDRGVGPGSVVGVCIERSPRMVAAQLAVLKA GAAYASLDPANPPARLAEMLADCRASLALTSSQASHKLTAAPCPVHLVQDGACAPSTHIP LVSRPDDLAYVLFTSGSTGTPKGVCVRHASLSRLVSFLHLRLDLSPSDRWTQVASSGFDA SVYEIWTPLACGAALLLADDDALRSPTALVSWLVAQRATLSFMPTPLAEACFEQDWTGSA LRAMTVGGDKLHPLRRPLPFRLFNMYGPTEATVITTVAEIADLGAEPPLGRPVDSALVYV LDPHMQPVPPGALGELYIGGACLAQGYTRTDLTAERFLPDPFGQPGARLYRTGDLVRWRP DGQLAFAGRRDEQVKLRGRRVELGEVESVLRRLPGVREGIVVLHGQGSAAHLIAHVVPDA HPPSERDLREGMARLVPDALVPAHFVLLPALPMSLSGKVDKKLLPAPPAAHADYEPPSGE LELELAHIWQSVLHLDRVGRHDSFFDLGGHSLLAMQVLGRIESSLGIRTTLRTLFEHPTL AQLASHLSSGAASTSAAAATALERGLTRPDGPSSPRVATPEEPFALTEGQRAMWLECQKS ADGALYNLGRTVRLGAGVDVAALRRAFEGLVERHEALRTTFLTRDGHPLQQVHRHVALEW AEEPAMALDEREIVARADEVRRRAFDLERGPLLRVHVWRRGEGQPPLLTVVVHHLVVDYW SFALLVRELGELYSALRAGRPPQLPPPSSFFAAGVSCPSPREAAGGAEYWRKALDGATTA

IDLPRDRARHDASPRRGRAHAITLPKPLTGALARLARERGTTLFSVLLSALTVLLHRASG QNDLVVGVPSAGRNDDESTRAFGYFVQMLPVRVALRGAASFDALVARVRDAFLDGLAHGD SALQHLLAEPRGAARRGGALFDVAFAFQGALPSLDPRLAALTTGAEDVRIAQGELELTTL

ADEQAAAEFDLALFAAELDSGIALRFEYDQQLFDPATIERMARHFVLLLESAVEHPGRPL SELRMLSDAERALLLDDWSGAAAARQAASAPAPACVHALFEAHAARQPDATALEFGHORF 10 TYAELSTWSTELALWLRDRGVGPGSVVGVCIERSPRMVAAQLAVLKAGAAYASLDPANPP ARLAEMLADCRAALVLTSSQASHKLTAAPCPVHLVQDGACAPSTHIPLVSRPDDLAYVLF TSGSSGTPKGVCVRHASLSRLVSFFQHLLALSPRDRWTQLASSGFDASVYEIWTPLACGA 15 ALLLADDDALRSPTALVSWLVAQRATLSFMPTPLAEACFEQDWTGIALRAMTVGGDKLHP ${\tt LRRPLPFRLFNMYGPTEATVITTVAEVADLGDEPPLGRPIDSALVYVLDPHMQPVPPGVL}$ GELYIGGACLAQGYTRTDLTAERFLPDPFGQPGARLYRTGDLVRWRPDGQLAFAGRRDEQ VKLRGRRVELGEVESALRRLPAVREGVVVLHGQGSAARLIAYVVPGADPPSERDLREGMA 20 10 RLVPDALVPAHFVLLPALPMSLSGKVDKKLLPAPPAAHADYEPPSGELERELAHIWQSVL HLDRVGRHDSFFDLGGHSLLAMQVLGRIESSLGIRTTLRTLFEHPTLHQLADRLSSGAAS TTAAAATVPASEIAPSLGRAPADEPYPLSYEQERLWVLEQLLPGGTAYNVVQAVRLRNLV DVDALSSALAALVRRHWSLRTVFVASPTPAQKICEPEAAPAEVVDLRGTPPDEAEAAARA 25 WASREQATGFDLARGPVFRARLFRLDHDVCVLVLSTHHIVTDAWSFQPLVRDLAELYRRA 15 RGGGPADMPELPLQYVDFAVWQRRFLAGKRLADKLAHWTATLRGLPVLELQTDRPRPPVQTFRGAERVLPLDARLVAQLDELARSRGATRFMVLLAALGVLLRRSSGQDDLAIGTAVANR 30 PRPELEPLVGFFVNTIVMRLDLGGDPTFEELLSRARKVALEAFEHQDAPFEKVVEAVNPR RDLSRSPLFQVMLVVQNAPTEALELGEVRIEPLDLPVEATRFDLRFSVEPRGGRDVISLO YNVDLFDAATIDRMLATMQSVLSRATQDPAQRVRALSVAPEDRERALVAWNDTAVATPDH LRLEEPFFERAVEQPDACAVVDAERRLTYGELARRAEAIAAAASRSGATANALVAVVMEK 2.0 35 GWEQVAAVLGVLRAGAAYLPLDPRLPEERLRHLLEHAEVRLVLTQSAVDGTIAWPAGIER LAVDADERWREQPVARRPPGGSTDDLAYVIYTSGSTGLPKGVMIDHRGAVNTVLDINRRF DVGPEDRVLALSSLSFDLSVYDVFGTLAAGGAVVIPDRTRASDPGHWRELVERERVTVWN SVPALMEMLMDASPGAGDPALSSLRLVMMSGDWIPLKLPDRIRAACRAPRVVSLGGATEA 40 SIWSIAHPIADVDPAWRSIPYGRPLANQHTYVLDEGLEPCPIGVPGEIHIGGIGVALGYW 25 RDEARTRERFLKHPTTGERLYRTGDLGRYFADGTIELLGRTDHQVKIRGFRIELGEIEAA LAQHPSVEQAVVAAKTDPSGEKRLVAYVVGADGDGAALRDFVRKKLPEYMIPAEVVVLPA 45 LPLSANGKVDRAALPDPAAVAPRAAAVAPRTATERLIASVLAEVLQVEAVGVTDNLFELG FTSLLLVRAQRLLAERIAARAPDEGAAAQAVSLTDLFQYPTIEQLAQRLDAATVKAEPAD 30 VGAORAEARRDARRRRGRG*

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Seq ID No 97 10 >Contigl1_011 544 amino acids MW=60164 D pI=9.10 numambig=0 ${ t MMSRIRAQLGVELPLRALFQGPTVAALAAQVDAARRGEARRREFPPIARIPRDGPLPLSF}$ ${\tt AQHRLWFVDQLEPGSPAYNIPFVVRATGRLDVDALRRSLFEIARRHEALRTTFSARDGVP}$ 15 FPVVAPEARVPFRMSDLEHLAGEALDAAVSALVLEESLAPFDLSRGPLLRVRV1RKRHDE HVIALVVHHVVFDVWSVGVFVGELAALYGGFAQGQPSRLPELPAQYVDFAAAQRAWLSGE VLEGELRYWTTKLSGALRRARVPVDHEPAGRRTWRGARRSLDAGAELTRQIKAFCEREAI SPFMALLAAYKLVLHQRTGLEDLVVGTDVANRNRVETEPMIGFFVNQLVLRTDCGGDPTF 20 GALVRRVRDVALEAFEHQDLPFDRLVEALRPKGAVGHVPLFDAKFVMRNVHVPPMKLEGL 10 ELEALEGEATTTAFDFVLTVAEAGGSFRFGVEHSSELYRAATVDNFLSDYRQILATATAR PDTPVSELRGELERAAAARRELERKAARGAALDKLTSARRAVTLPRPGAPGEAKTSPKD DLDE* 25 15 Seq ID No 98 >Contig12_001 514 amino acids MW=56145 D pI=8.82 numambig=0 30 PPAVRRYVADRRPEQLPALAPEEREAAARRLSALGAAPPQVRRRGLTRAPLSYGQSRIYF LEQLSPGKPLFNVPGAVRLRGPVDVARLSAAFGEIVRRHDALRTSIANVDGELLQIAQPH AGFALDVVTSTPEEAAELDRRLRAEAWRPFAIGAPPLLRATLFRLAEDEHVLLVTMHHVV SDDWSLGVILRELLALYAGRSLPPPRLQVSDFAAWQREMVESGALDGQRAYWRERLRGLS 20 35 RASISAGGGAEAPSHDPSGAIEEIALSPDKAAALEALARREGATLFMVLLALLDLVIHAR SGALDIAVGTPIANRNRPELEDVVGLLTNTLVIRVDLARAGAFRDVLARARVQALDAFAN QDIPFDVVTQDLKQERDHAQHPLFRVWLALQNAPKPALEVRGLRVEPLPLRPELVHFEVA

ARAQAALGEAFARAATARLGQLRRRSAGDRTPRE*

Seq ID No 99

>Contig12_009 582 amino acids MW=65555 D pI=8.72 numambig=0

MREPSSTPNWRNFGSNLPAGSDSVPPGEGFPIKKILALNLGKWKDTAGLQIAQALHLFEY
GYKRYREGKFVLRATSDLGLGAIFESIDNWESFDQFEEFFKPWTFIRKPLVATRWAEDAE

LLLWPADDGSVVGHFEFRRDRVDEGARKEIAAAFTHLVDAVIARPDAPVSTLVEGARAEA

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FGRQRLVGINPAHIRRATPADLADFVSGAEPKPIAIADGRTLEEVREGGQLYFLDYRIFK
DIVDTDVQEELGKYPLAPTCMLHQTAAGELLPVAIRLVHSRPGKGAHPDKIFTPSGPSDD
WLTAKIAVASADAIYQGQVTHLLYAHLIVEPFAVSTYRNLPATHPLHQLLRPHFFNTLAI
NELARRRFLGRGRFFDITSSVATMGSFELLTRAYTGKGIKGYGGKPWRFYESALPRDLSA
RDVRDLVGYHYRDDALLHWDAIQEYVGQVLKIAYPTPGSLSSDASLQRWIHELVSPQLGG
MDSLLPPERADQLEKLTSLDDLIAIVTNIIFTATAYHAAVNFGQTDYYTWIPNAQFATYR
SYGDVLNGSEKRQFKPLERLPGRAQSIRQMVLSRSLSMGPPLTSESLMTMKCLLQDPAAK
QAFARYRERLAHIEREITERNRAREQPYLYLLPSMVPQSVAI*

SEQ ID NO 100 (>ORF1)

VSQRTSCYLRGGGVCSMNDAFLALERNERNRPSTVIDLLRQRAEAEPARPIYCFLESGDVEAG

ATWVTLREIDERARTVAALLQASGVAPGARALLLYPPGIEYITAFFGCLYAGVRTVPAYPPDL

GRLERTLPRVASIVADARAEAALTSSAVAGIVASLPASAAAAALQRLRWIATDGPSPGPIEGP

GAALRPESVAFLQYTSGSTGEPKGVMLTHGNLLHNSRLIAHGFDLTSPDPVGVIWLPPYHDMG

LIGGILQALYRRIRVALMSPLSFLQRPMRWLRAVSALGASVSGGPNFAYDLCVRKSSEEERAA

LDLRSWEVAFTGAEPVRADTLDRFARAFAVSGFRREAFYPCYGLAEATLIVSGGARAEAPVLA

RLAPEEVELGRAVASAAEGARVFVGSGRALDPRAVAIVDPAGNELGPGEIGEIWVSGPSVAVG

YWGRPEETEATFGATLAGSAAPRYLRTGDLGFLRGGELFVVGRSKDLIILRGRNHFPQDIEKT

VESSHRAVRPGCSAAFSVEHEGEERLAVVCEVDPRVAADPREIVAAREAVTAEHQLVAHAVAL

IAPGALPKTSSGKVRRRECRRAFLEDALGERHVAFAPELLDDASPPDDAPPETEEPSGRSLLD

ALRSTLARALRLDAGQIDDALPISRFGLDSLAAVELQHAFQVRTGRAIPLTSILRGGSLRLTR

EITRLDGPSSPRVATPGGAVCADRWGTGRFGSSAISRPMERFTTWAGRSGSVPAFKRVDLRRA

SEQ ID No 101 (>ORF2)

VYSSAYVLFAVCAGTTRVASAPETAGFPLECVGDDGTVLGPDSFVVGYTQVYVFKKERLNTNP
PIDGFTLKLDGNEVAPGEDGLPVVKRCVRSEEQACGCGRTEPAEDECTTYEIEAVVPEKAAEV
DEEAAGLGGPPAREAIWVDYYTDGGEFDGARRLVSDTTGASRGGNGTTWTPPSEPGRVSLWAV
VHDTRGGASVTRREVOVE

1.0

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SEQ ID No 102 (>ORF3) VVGTVLSAGTGEPLPD1AVTLVRPDGGREEAKTDQGGKFRFKNLPPGKYRVEVAAAGFEPFAA 10 EEEIAAGEAIEVRYRISLAAPQDGKAPGIEVTVQGERPPREVTRRTIERREIDRIPGTGGDAL RSLQSLPGVARSGFGLLIVRGSAPQDTLTFVDRTPVPIIYHFGGLSSVVPTEMLEKIDFYPGN ${\tt FSAVYGRAMGGIVDVGLRSPKQDGKYHGVVQLDLIDGRVLLEGPVPFLKDWTFIAAGRRSWVD}$ 15 AWLGPVLKEAGSSVTQAPVYYDYQFVLEGRPSASERVRASFYGSDDAFKITLDKPPEDEPALT GDFGLHTAFQRFQLSYENRIGSRDRLLWSMALGRDIADFEISPLAFNVVSTSLDLRLELSHRF ARYLTMNVGTDLSGGVATVNIRAPSQQPAGHPSNQPFSTYPFQDRSFDGAYSRPAAYAELEVV PSPRARIVPGVRVDYALDTQTLDVSPRVNARYDIRSGFPRTTAKGGVGLYYQAPQFAESIEPF 20 GNAELKSNRAVHYGLGVEQEITPQIEVTLDGFYKQLDRLVVFSPEKDDYADGTGYAVGGELLL 10 KYKPDERFFGWAAYTLSRSVRKDGPDEEEHLTQFDQTHVLTVLGSLRLGRGWELARFRLVSGN LQTPYVCDPEEKGCNPNRVNAIYHASSARYSPIPLGGDYSERMPLFHQLDIRADKTWKFKRWO $\verb|LGLYLDIQNVYNYMAAEGISYNFNYTKREYVTGLPFLPTLGLRGDF|$ 25

15 SEQ ID No 103 (>ORF4)

VIAVDNNPEAVDAVKDKTSAAFVGDATVHKVLEGIGAQYVETAIVTFGEHFEPSVLCVASLVR

MGVRIIARAATDRQADILRAVGATRVIQLETEMGRRVGADITMPLAQDLLDLASHYRVVPWNA

HGPLVGQTLAGSKIRQRYRINVLGVRPHTNKRPGDKPRLEAPTPDYVIRDGDTLLLVGDSDDV

SEQ ID No 104 (>ORF5)

SGSSGGGSSAEGSRCQPSGGGPHWLLEGETVTFPVTCASGLALAGDAFEVGPLPEGAAYDPIA
REVTFSPGLDQAAVYDIEIRVAQTSEVGRVKVGVADAFADPSNVPVVDPTRYPEEYGLPVLFL
SPVPEDKEYAPATVIYRGHTYAAEAELRGESSLSYPKRSYTLKFPKDDKFNEPDEAGGFTDRR
KVVLITTFDDNSYVRQRLAYDLWNRLDPEHIQIKTYSAVLYLDGEYAGLYTVADHVDGYLMED
HGYPQDGNLYKAVSHDANFALTDRSGDPKDTLHDGFEKKEGAPAEGEPEAFSDLEDLVSFVAE
SDDATFAAEIGSRIDLRDYEDWWIFVTFIVANDSAGKNSYHYRDPAADGVFRYAPWDFNASFG
QSWETEREPASDRVDYRDVNLLFERLLEEPSIGDPLRARYDQVLRGALAEAEIHAIVDGYVER

IDASARRDEARWGEAYRSYEGWSWRDDFTTYEEEIAYLK

30 AWISERWQHQDELY

SRFVAEVGG

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SEQ ID No 105 (Contig 11 >ORF1) 10 VLDVWSTSDQVACRLHCAGAGPSASLELRYDASAGARRDAERLAERLAALLEDLSRHPERPVA QGEVGPGERAEIEAWSRGPAMELPSACALHRWFEERAEQHPDVVAVRSEGKSLTYGELERRAN ${\tt RLASCLRRGVGLDTIVGVCVPRSEDMVVATLAVLKVGGAYLPLDHEYPGERLAFMMRDARAR}$ LLVTHDAIADELPTGGWTTLLLDAEAAEIAACSDARPAVSPPPDSGAYVIYTSGSTGTPKGSL 15 ISHRAIVNQMQWIQRYWALTADDRVLLKAAFGFDVSVWEIFWPLSFGARIVVARAGGHRDPEY LRRLVRDEGATTAYFVSSMLAAFLGGPEQPFPASLRKVLVGGEAVPLDLVRRFYAKHDGDLIN MYGPSEAAIAVTGCVLPSDPRVTWVPLGAPVANAEVFVLDGAMRRPAIGALGDLYIAGAPLAR 20 10 ${\tt GYVGQPGLTAERFLPDPCARAAGGRMYRTGDVARFLPDGMLEFQGRSDHQIKLRGHRIELGDV}$ EAQIRRVPGVGQAAVVLREDAPGDARLVAYVVLDGDAAGDAPDVRAGLKASLSAYMIPSSVVR LYALPMCSERLAFTGSSYAGCLL 25

223

SEQ ID No 106 (Contig 11 >ORF2)

MSDHEMTGFSLSPQQRAIRALDREAGAPGCRTLAVVAVTGPCDEGRLSAAALALAERHEILRT
RLVEGRARPRRWSASRASRGRQQDDWVGCSEAEQGERMSRLVARLSEDRGADDGLRVGLVRVG
PEERRLVLAAPAWCVDEESIAPLVRELCASTAGAGAPPEQQYADVAEWLNGMLESEDAGDGRR
FWAERRSHFGPPLHLAFSRGGAGAGAGSGRARVDLQGGMAQVERWSSSWQVPQRIVLLALWAS
LLWRMSGGNEPEVTVAVRFDGRSLDALAGAVGPFARFLPVRIEISASDTLADVARRLALAEAE
20 AAAHODAAPGVSHRMSWGLLRRGGBAGAVARPRAGDBARLEUV

20 AAAHQDAAPGVSHRMSWGLLRRGGRAGAVARRRAGPRARRLEHV

SEQ ID No 107 (Contig 11 >ORF3)

MSRIRAQLGVELPLRALFQGPTVAALAAQVDAARRGEARRREFPPIARIPRDGPLPLSFAQHR
LWFVDQLEPGSPAYNIPFVVRATGRLDVDALRRSLFEIARRHEALRTTFSARDGVPFPVVAPE
ARVPFRMSDLEHLAGEALDAAVSALVLEESLAPFDLSRGPLLRVRVIRKRHDEHVIALVVHHV
VFDVWSVGVFVGELAALYGGFAQGQPSRLPELPAQYVDFAAAQRAWLSGEVLEGELRYWTTKL
SGALRRARVPVDHEPAGRRTWRGARRSLDAGAELTRQIKAFCEREAISPFMALLAAYKLVLHQ
RTGLEDLVVGTDVANRNRVETEPMIGFFVNQLVLRTDCGGDPTFGALVRRVRDVALEAFEHQD
LPFDRLVEALRPKGAVGHVPLFDAKFVMRNVHVPPMKLEGLELEALEGEATTTAFDFVLTVAE

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AGGSFRFGVEHSSELYRAATVDNFLSDYRQILATATARPDTPVSELRGELERAAAARRELERK AARGAALDKLTSARRRAVTLPRPGAPGEAKTSPKDDLDE

SEQ ID No 108 (Contig 11 >ORF5)

MSEPIETEDGGSDIAIVGMAGRFPGAPSVDALWENVRRGVESIARFPESEREEPPVGASAAPG
APVVCAGGLLDDIDRFDASYFGYSPREAQLMDPQQRLFLECAVAALEDAGCDPARFPGAIGVF
GGCGSNTYLLQLLSHPDLAATVDPHALMLASEKDYLATRVSYKLDLHGPSVVVQTACSTSLVA
VHMACESLLGGQCDLALAGGVSIGIPQKRGYPYVPGSICSPDGRCRPFDARAEGTVGGSGVGI
VALKRLADALRDRNTVHAVIRGSAVNNDGGRKVGFMAPSVDGQAAAISEAQSVAGVDPGSIGY
VEAHGTATAIGDPIEVEALTQAFRRKTPRKAYCALGSIKANIGHLDAAAGVAGLIKAAHVVRS
GEIPPCVHFEAPNPKLDLAASPFFVPREAAPWPRELRPRRAGVSSFGIGGTNAHVVLEEPPPL
PPRAPAPERDHVLTLSARTPEALSTACAQLAAHLEATDVPLDDVAFTLQTGRAEHPYRRAVVA
RTRAEAIQGLAREGASALARPDEPRPSSRSRARARRPSGWPARSTRRRRSGAPSTRARRRRGR
AASISARSSSARARATGARCSAPRWRSPRSSPSSSRSPGSG

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SEQ ID No 109 (Contig 11 >ORF6)

VVDHHVVVEYWSFALIVRELGELYSALRAGRPPQLPPPSSFFAAGVSCPSPREAAGGAEYWRK
ALDGTTAIDLPRDRARHDAGARRGRAHAITLPKPLTGALARLARERGTTLFSVLLSALTVLLH
RASGQSDLVVGVPSAGRHDDESARAFGYFVQMLPVRVALRGAASFDALVARVRDAFLDALAHG
DSALRHLLARAQGEAQRDALFDVAFAFQSTPPSLDARSALAIGVGDVRIAQGELELTTLADEQ
AAAEFDLALFAAELDAGIALRFEYDQQLFDPATIERMARHFVVLLESAVEHPGRPLSELRMLS
DAERALLLDDWSGAAAARQAASAPAPACVHALFEAHAARQPDATALEFGHQRFTYAQLSTWST
ELALWLRDRGVGPGSVVGVCIERSPRMVAAQLAVLKAGAAYASLDPANPPARLAEMLADCRAS
LALTSSQASHKLTAAPCPVHLVQDGACAPSTHIPLVSRPDDLAYVLFTSGSTGTPKGVCVRHA
SLSRLVSFLHLRLDLSPSDRWTQVASSGFDASVYEIWTPLACGAALLLADDDALRSPTALVSW
LVAQRATLSFMPTPLAEACFEQDWTGSALRAMTVGGDKLHPLRRPPFRLFNMYGPTEATVITT
VAEIADLGAEPPLGRPVDSALVYVLDPHMQPVPPGALGELYIGGACLAQGYTRTDLTAERFLP

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30 APPAAHADYEPPSGELELELAHIWQSVLHLDRVGRHDSFFDLGGHSLLAMQVLGRIESSLGIR

DPFGQPGARLYRTGDLVRWRPDGQLAFAGRRDEQVKLRGRRVELGEVESVLRRLPGVREGIVV LHGQGSAAHLIAHVVPDAHPPSERDLREGMARLVPDALVPAHFVLLPALPMSLSGKVDKKLLP

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 ${\tt TTLRTLFEHPTLAQLASHLSSGAASTSAAAATALERGLTRPDGPSSPRVATPEEPFALTEGQR}$ AMWLECQKSADG 10 ALYNLGRTVRLGAGVDVAALRRAFEGLVERHEALRTTFLTRDGHPLQQVHRHVALEWAEEPAM ALDEREIVARADEVRRRAFDLERGPLLRVHVWRRGEGQPPLLTVVVHHLVVDYWSFALLVREL GELYSALRAGRPPQLPPPSSFFAAGVSCPSPREAAGGAEYWRKALDGATTAIDLPRDRARHDA 5 15 SPRRGRAHAITLPKPLTGALARLARERGTTLFSVLLSALTVLLHRASGQNDLVVGVPSAGRND DESTRAFGYFVQMLPVRVALRGAASFDALVARVRDAFLDGLAHGDSALQHLLAEPRGAARRGG ALFDVAFAFQGALPSLDPRLAALTTGAEDVRIAQGELELTTLADEQAAAEFDLALFAAELDSG IALRFEYDQQLFDPATIERMARHFVLLLESAVEHPGRPLSELRMLSDAERALLLDDWSGAAAA 20 RQAASAPAPACVHALFEAHAARQPDATALEFGHQRFTYAELSTWSTELALWLRDRGVGPGSVV 10 GVCIERSPRMVAAQLAVLKAGAAYASLDPANPPARLAEMLADCRAALVLTSSQASHKLTAAPC PVHLVQDGACAPSTHIPLVSRPDDLAYVLFTSGSSGTPKGVCVRHASLSRLVSFFQHLLALSP RDRWTQLASSGFDASVYEIWTPLACGAALLLADDDALRSPTALVSWLVAQRATLSFMPTPLAE 25 ACFEQDWTGIALRAMTVGGDKLHPLRRPLPFRLFNMYGPTEATVITTVAEVADLGDEPPLGRP 15 IDSALVYVLDPHMQPVPPGVLGELYIGGACLAQGYTRTDLTAERFLPDPFGQPGARLYRTGDL VRWRPDGQLAFAGRRDEQVKLRGRRVELGEVESALRRLPAVREGVVVLHGQGSAARLIAYVVP GADPPSERDLREGMARLVPDALVPAHFVLLPALPMSLSGKVDKKLLPAPPAAHADYEPPSGEL 30 ERELAHIWQSVLHLDRVGRHDSFFDLGGHSLLAMQVLGRIESSLGIRTTLRTLFEHPTLHQLA DRLSSGAASTTAAAATVPASEIAPSLGRAPAD 20 EPYPLSYEQERLWVLEQLLPGGTAYNVVQAVRLRNLVDVDALSSALAALVRRHWSLRTVFVAS 35 PTPQKICEPEAAPAEVVDLRGTPPDEAEAAARAWASREQATGFDLARGPVFRARLFRLDHDVC VLVLSTHHIVTDAWSFQPLVRDLAELYRRARGGGPADMPELPLQYVDFAVWQRRHLAGKRLAD KLAHWTATLRGLPVLELQTDRPRPPVQTFRGAERVLPLDARLVAQLDELARSRGATRFMVLLA ALGVLLRRSSGQDDLAIGTAVANRPRPELEPLVGFFVNTIVMRLDLGGDPTFEELLSRARKVA 40 25 ${\tt LEAFEHQDAPFEKVVEAVNPRRDLSRSPLFQVMLVVQNAPTEALELGEVRIEPLDLPVEATRF}$ $\verb|CLRFSVEPRGGRDVISLQYNVDLFDAATIDRMLATMQSVLSRATQDPAQRVRALSVAPEDRER|$ ALVAWNDTAVATPDHLRLEEPFFERAVEQPDACAVVDAERRLTYGELARRAEAIAAASRSGA 45 TANALVAVVMEKGWEQVAAVLGVLRAGAAYLPLDPRLPEERLRHLLEHAEVRLVLTQSAVDGT IAWPAGIERLAVDADERWREQPVARRPPGGSTDDLAYVIYTSGSTGLPKGVMIDHRGAVNTVL DINRRFDVGPEDRVLALSSLSFDLSVYDVFGTLAAGGAVVIPDRTRASDPGHWRELVERERVT

VWNSVPALMEMLMDASPGAGDPALSSLRLVMMSGDWIPLKLPDRIRAACRAPRVVSLGGATEA
SIWSIAHPIADVDPAWRSIPYGRPLANQHTYVLDEGLEPCPIGVPGEIHIGGIGVALGYWRDE
ARTRERFLKHPTTGERLYRTGDLGRYFADGTIELLGRTDHQVKIRGFRIELGE1EAALAQHPS
VEQAVVAAKTDPSGEKRLVAYVVGADGDGAALRDFVRKKLPEYMIPAEVVVLPALPLSANGKV
DRAALPDPAAVAPRAAAVAPRTATERLIASVLAEVLQVEAVGVTDNLFELGFTSLLLVRAQRL
LAERIAARAPDEGAAAQAVSLTDLFQYPTIEQLAQRLDAATVKAEPADVGAQRAEARRDARRR
RGRG

SEQ ID No 110 (Contig 12 >ORF1)

10 PPAVRRYVADRRPEQLPALAPEEREAAARRLSALGAAPPQVRRRGLTRAPLSYGQSRIYFLEQ
LSPGKPLFNVPGAVRLRGPVDVARLSAAFGEIVRRHDALRTSIANVDGELLQIAQPHAGFALD
VVTSTPEEAAELDRRLRAEAWRPFAIGAPPLLRATLFRLAEDEHVLLVTMHHVVSDDWSLGVI
LRELLALYAGRSLPPPRLQVSDFAAWQREMVESGALDGQRAYWRERLRGLSRASISAGGGAEA
PSHDPSGAIEEIALSPDKAAALEALARREGATLFMVLLALLDLVIHARSGALDIAVGTPIANR
NRPELEDVVGLLTNTLVIRVDLARAGAFRDVLARARVQALDAFANQDIPFDVVTQDLKQERDH
AQHPLFRVWLALQNAPKPALEVRGLRVEPLPLRPELVHFEVALLLWPADDGSVVGHFEFRRDR
VDEGARKEIAAAFTHLVDAVIARPDAPVSTLVEGARAEAARAQAALGEAFARAATARLGQLRR
RSAGDRTPRE

20 SEQ ID No 111 (Contig 12 >ORF2)

MSIHIEEEGRADAAKAPPFDYLQALHSALAHENDPVKRKQIEAGMVFKWLREEFLPFLSQLRR

EKPIFSIPAITLVTRYNDVVEVLNANDVFSVDNIAPKLVENVGQNILAMNDSPKYEHEKSLLR

LAFPRADLPRYRQIVVDEANRLLAKVGVDKPFDLTGDYALRVPAGAMARYLGVGEIPTEKVVA

WTHALFNEIFLNPTNDPTAVAAARAARQEALPMIDAIVAARKKQLAKSPPPEQFSVLDRYLVM

25 QSVPETYESDEGIRDVILGLLMGCVDLSGGAIVNALVELMKRPRVLRDALNVVNVEDDAAITG

YVLEALRFRPPSTGVTSLCVRDYTVGRGTRHEEKVPAGALVMACSASAMHDHEHIDAPDQFRP

GRLPSRNYLFWESGIHTCHGKYVAILHISLAIKQLLRAGVPSAIDPMPRVHGYPAPFRVRLAA
AEG

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SEQ ID No 112 (Contig 12 >ORF3) MREPSSTPNWRNFGSNLPAGSDSVPPGEGFPIKKILALNLGKWKDTAGLQIAQALHLFEYGYK 10 ${\tt RYREGKFVLRATSDLGLGAIFESIDNWESFDQFEEFFK?WTFIRKPLVATRWAEDAEFGRQRL$ VGINPAHIRRATPADLADFVSGAEPKPIAIADGRTLEEVREGGQLYFLDYRIFKDIVDTDVQE ELGKYPLAPTCMLHQTAAGELLPVAIRLVHSRPGKGAHPDKIFTPSGPSDDWLTAKIAVASAD 15 AIYQGQVTHLLYAHLIVEPFAVSTYRNLPATHPLHQLLRPHFFNTLAINELARRRFLGRGRFF DITSSVATMGSFELLTRAYTGKGIKGYGGKPWRFYESALPRDLSARDVRDLVGYHYRDDALLH WDAIQEYVGQVLKIAYPTPGSLSSDASLQRWIHELVSPQLGGMDSLLPPERADQLEKLTSLDD LIAIVTNIIFTATAYHAAVNFGQTDYYTWIPNAQFATYRSYGDVLNGSEKRQFKPLERLPGRA 20 10 QSIRQMVLSRSLSMGPPLTSESLMTMKCLLQDPAAKQAFARYRERLAHIEREITERNRAREQP YLYLLPSMVPOSVAI SEQ ID No 113 (Contig 12 >ORF4) 25 VSSSRSTGRVPRDRASPAGSCAPALVPGPPLSYASVMPPLDLHVALFGASGAGKTVLLAAFYR AQTQPSFQQEYAYKIQAVNKAQGNQLLGRFYRLEEGRFPDGSTRFDEYEFDFFPRDLPEPAVR 15 IHWYDYPGRWWEDEPVDADEREAMRQGLIRLGMSQVGILLADGAKYRAEGTGYIRWLFEHFAD ECDRLRRASAATGDEVSFPREWILALSKADLCPPDYSARDFEREVCRDADDQLAKLCSVLRAE 30 HAFGHRFMLLSSVAAPAGAQVDPRTSLGVRTLAPAILVSTVEGAVREAQAARKEKSAGETFFO GLRDLVQFVDSLDDFLPKRYQIVSKILRFISIKDFATTRLDRLKKMREDAIRKGDTFTAVLTA 20 MVAALRDDEGARAYHONO 35 SEQ ID No 114 (Contig 12 >ORF5) MPAPAPLVETSRLLWRTRGEHWDYEFICVPEIPALPAWLSTLEAMLADADAGAGELRYGLLEI DDRGQRAPRAYPYVAVRFLDPARRDWTGRQVQHFAAWFPPVPPEAVAELPEAVPADWHLRVLD 40 GLAGTYGSGEVFGLPEATIRAWKRSHDESRAARAMAIVKATPPVSLGGGEAAPSRWTRVPTLK 25 KKPPEPPAAAGLLSVGAVPSGQGRRFGCFAIGAMMLAAFCRLMLACGVRLLGA 45 SEQ ID No 115 (Contig 12 >ORF6) VRFRSSLGPLLLAALGAALTVSAAFRSAEASVFDSASRWPEDADGHVRIPVCIDPTSSAEQRV ${\tt DGAAGGLIHAPNPSLADVITRVRTALQGSWERWSSVRFTGWESCDSLLPATRMTYVGVRIHPD}$ 50

APNQSDSIGVYNKGGSVQFKPWGADFNRCIKYNWQTARVEYSFDCVEQYAIHEMGHAIGFMHE WHHPLVPSACSQREPLPASDVASGWPSSRRYIVVNPGFYDYDSIMTYWSGCSDQDGVRFGSET . 10 LDAVDIQAVATVYPPVGGAPDVCNPGWFAGKRWFCAAQPTVSVGNSCSSGWVECLPHCNPRPF QGEWWTCPTNPYAVTGQSCSARWELCGD 5 SEQ ID No 116 (Contig 12 >ORF7) 15 VGESQGALVGGNALSTNALNLNALNLNALNLNALNLSGLSARNLAAIQDPGPSGALARDFLRY ${\tt AASCALSSTASFDFSWTDSNGKRHDERYPGLLGVAPAWASGPLDDAGQRIVSSCVAARVNYYQ}$ VPVLLSARSLRDPLKTLSSSQELIDYPDVEGAFWGNLFAAQPYINACYNSATVDNSRAYQRDC 20 10 AAGHVTSGGQIVECGLIRIAGSCDRVCQKLNGAGQYYPSCVDRPGQSTATTKDVITTALP SEQ ID No 117 (Contig 12 >ORF8) VLAAHCERGGLTARAASLLARGAELAAARRAYLDAEGCYGRVEALLGALLPEERRARGLARFR 25 LGRHTEALADLAAAREAAAAASEAGAEIELLLDEAMILDWTGEYRAARERVAAAERLAGRVAS 15 PLLGARLLLGVGRSLHRADREDEAAAVLTRAAAQAARLGDEGHETHIIALLLLGFILASLGRV EEAARDLDAVILSCEERSDLMHLGAALNNRGLARALQGDRAGMIADFERTIALGRELGQPAFE 30 LVGRYNLAEYLYLMDDLAAARPHARAVQAIAPRCGDRHAPVVVTLLIARLRLYQGDEAGARRI ALRLRAARDDAGCEALKPSEDVLCAMIELATRDDDRAAWAALEERSARCSVGQERIEVLEARA LAALRRGRRADARAQLERALAAASTIPTVMGGRLRRWYAELTRATESDAPDIDLAAAEATFTG 20 ARAREKVEY 35 SEQ ID No 118 (Contig 12 >ORF9) QAYPDLWAERGRQELWLRQLPPRACAQLAREALGDAADGALIDRLVTQSEGQPFFLEELIRAT AEGRGDALPETVVAMVQVRLEALAPPARRILRAASVLGEVFWRGAVAHLLGGDEAAPLAEHLS 40 $\verb|ALVAGELCVRHREGRFPGEEEYSFRQALLREGAYAQLTKDDRALGHRLAADWLEAAGEADPLV|\\$ 25 LAAHCERGGLTARAASLLARGAELAAARRAYLDAEGCYGRVEALLGALLPEERRARGLARFRL GRHTEALADLAAAREAAAASEAGA£IELLLDEAMILDWTGEYRAARERVAAAERLAGRVASP LLGARLLLGVGRSLHRADREDEAAAVLTRAAAQAARLGDEGHETHIIALLLLLGFILASLGRVE 45 EAARDLDAVILSCEERSDLMHLGAALNNRGLARALQGDRAGMIADFERTIALGRELGQPAFEL

VGRYNLAEYLYLMDDLAAARPHARAVQAIAPRCGDRHAPVVVTLLIARLRLYQGDEAGARRIA

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LRLRAARDDAGCEALKPSEDVLCAMIELATRDDDRAAWAALEERSARCSVGQERIEVLEARAL
AALRRGRRADARAQLERALAAASTIPTVMGGRLRRWYAELTRATESDAPDIDLAAAEATFTGA
RAREKVEY

- 5 14. DNA sequence according to any of claims 1 to 5 wherein the DNA is selected from the group consisting of
 - (a) the following DNA sequences:
- 20 10 Seq ID No 119 (>Contig17) TCGAGCGCGAGCGGACGACGTCGGCGCCGCCTCGGTGAGCGCCGCCGC GAGGGCGCTCGCGAGATCGCTGGCGACGCCGGGCCGGGGCCACGACGAGCC 25 ACGTCCCCGCGACGTCGCCGCGTGACGCGCGCTCACGGGTCTCCATTCG 15 ACGCGGTAGCGCCACGCGCCCACGGTGCTCTCGCCGCGGCTCCGCCG CCACGCCGACAGGGCCGCCATGAGGCTCTCGAGGGCCGAGCGCCCCCCC 30 ATGGCTCGCCAGAACGCGGTCTCCTCGGCGGACGCTCCCGGCGCCGCGTC CTCATCGTCCGACGCGTCGCCTGCGTCGAGCCAGAACCGCTCGCGCTGGA ACGCGTACGTCGGCAACGTCACGCGGCGCGCCCCGAGCGGAGCGAAGAAC 35 GCACCCCAGTCGATGGCGTGCCCGCGCGCGTGGAGCTCGCCTGCCGAGAG GAGGAAGCGCTCGAGGTCGCCTTCGTCGCGGCGGAGCGAGGACACCACGG TCGCATCGCCGTCGATCGACGAGGGCGTCTCGTCGAGCGCGACGGTGAGC ACGGGGTGAGGCTGACCTCGACGAAGAAGCGGTGGCCGTCGTCGAGCAG 40 GGCGCGCGTGCTCGAAGCGGACGGTGTGGCGCAGGTTTCGGTACC 25 AGTGGGCGCCGAGGGCCTCGCCATCAAGCCTCTCGCCCGTCACCGCG

30 AGCTCGTCGATAGCGCCGGGGTCTCCGGAGACGAGGGCCGCGTGAGGGCT

GASTAGAGCGCCACGGTCGCCGGGCGCGCGATGCCGTCGAGCGCCTC

 ${\tt CAGCATCGTCCGATGGCCTCCACGTGGGCGGAGTGGGAGGCGTACT}\\ {\tt CGACGCGGACCTTGCGGCGAACAGCTGCGCCCCGCTCAGCTCTGCGACG}\\$

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GTTGATCGCCGCTATCGCCAGGCGTTCGCCCAAGGGCGCAAGGCGCGCCT CGAGCTCGGCGTGGTGAGCTCGACGGCGGACATGGCGCCGCGTCCCGCG 10 AGCTTCGTAATGGCGCGAGCGGAGCGCGACCCTGGCGGCGTCTTC TAGCGAGAGCGCCCCGCGACGTACGCGGCCGCGATCTCGCCCTGGCTGT GGCCGACGACCGCGTCGGGCGTGACTCCGGCGGCGCCCAGGTGGCGGCG 15 AGGGCGATCATGACGGCGAACAGCACGGGCTGCACCACGTCGACGCGCTC GAGCATGGGCGCGGCGTGCGCTTCGTCGCCGCCGAGCACGGCGAGGAGCG ACCAGTCGACGTGCGGCGCCAGGGCGCTCGCACGCCTCGATCTCGGCC CGAAAGGCGGCGAGGAGCGAGCAGCGCGCCATCGATGGCCACTG 20 10 CGAGCCCTGGCCGGGGAAGACGAAGGCGACCTTGCCCGGCGGGGGGCGCCT CGCCCGCGACCGTTCCTGCCCCCGCGCGCCCCTCGGCGAGCGCCGCGAGC GAAATGCGACCGCGTGGTCGCGAGCGACGCCGACGTCGACGAGGGCGA 25 CGTCCTCGTGCTCGGCGAGGTGCGCGTGGAGCTTGCCCGCCTGAGCGCGG 15 AGCGCCGCGTCGCTCTTCGCCGAGAGGAGCACCGGCACCGGCGCGCGAA 30 GCGCTTCCTCGAGGACCACGTGCGCGTTGGTGCCGGAGATCCCGAACGAC GACACCGCCGCGCGAGGAGACCCGCCTGGCTTCCACGGTACCTCCTC GGTCAAGAGGCGGATCGCCGCCGGACGACCAATCGATGTGCTGCGACGGGC TCGCGGCGTGGAGCGCCTCTGCAGCGCGAGCACC 35 ATCTTGATGACGCCGCCGATCCCCGCGGCGGCCTGCGTGTGCCCGAGGTT CGACTTTAGGCTCCCGAGCCACAGCGGGCGCTCCTTCGCGTGCGCCGCGC CGTACGTCGCGAAGAGCGCGCGCGCCTCGATGGGATCGCCGAGCGTCGTG 40 GCTCGCGAGCGCGTCCCGGATCACGCGCTCTTGCGCGGGGCCGTTCGGCG CCGTGAGCCCTTGGCTCTTGCCGTCCTGGTTGACGGCCGATCCGCGCACG ATCGCGAGCACGGGGTGCCCGTTCTTCCGGGCGTCCGACAGGCGCTCGAG 45 GAGCACTATCCCAGCGCCTTCCGACCAGCCCGCGCCGTTCGCGTGCGACG TCGCCGAAGATCCCGGGGGGTCGCCATCACGGTCACGCCGCCGGCGAGCGC

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GAGCGAGCACTCGCCTCGACGGATGGCGTGGCAGGCGAGGTGGAGCGCGA CGAGCGACGAGCTGCACGCCGTGTCGACGCT

Seq ID No 120 (>Contig18)

5 TTTTAGGANCCCCGACGTGCACGATCGGCTCGCCAACCTCGTGGCGCGCC GGGACTATTTTTACCAGCTCGCGTTGCGCGCCGCGGGGACCTACGTGCGG GGCCTCGTCCGCGCCCCGCACGACGGCGCGCGCCCCCCCGCGTTCGCGCC TTGCCCGTTGGTTCGCGCGGATCGGCGCCGAGCACATCGTGCTCGCGAGC CGCCGCGGAGCCGCGCCCCGGCGCGCGCGCCGCGAGGAGCTTTC GGTGCTCGGCGCGCGCGTGACGCTGGTTGCGTGCGACGTCCCCGATCGTG AGGCGGTCGCGGGGGCTCGTGCGCAACGTCAAGGCCGGCGGAGCGACGGTG CGCGCCGTGTTCCACGCGGGCGGTGCGATGCACGAGGCGCCGGTCGCCGC CATGCGTGTTGAGGAGCTCGCCGACGCGATCGCCGTGAAGGCCCGCGGCG 15 CGCAGCACCTCCAAGACGTCTTCGCGCAGCGCCCGCTCAACGCGTTTGTC CTCTTCTCGTCAGAAACGGGTGTGTGGGGGGGGGGGGGCGCGTA CGCCGCGGCGAACGCGTTCCTCGACGCGCTCGCCGAGGCGCGTCGCGCGG ACGGCCTCGCGGCGACCTCGATCGCGTGGGGCGCGGCGGCGGCGGA ATGCTCGCGACCGACGCGAGCGGCGCTTGAAGCATCGCGGCGTCGCGCC GATGGATCCGGAGCTCGCGTCGCGCCCTCGCGCACGCGCTCGATCACG CCGAGACGTGCCTCGCCGTCGCTGACGTCGACTGGGCGCGCTTCGCCCCG TCGTTCGCCTCGGCGCGTCCTCGCCCGCTCCTCGACGAGCTCGCGGAGGC GCGATCGGCGCTCGACGCGCTGCGCGAGCCACCGGACGACGCGCGCACGG CCGCCGGTCCCGAGCCCGCAAGCACGCTGAGGACCACGCTCGCGGCGCTC - GGCGGCGGTGCTCGGGCACGCGGACGCGTCGCGCGTCGAGCCGAACCGCG GGTTCTTTGACCTCGGGCTCGACTCGCTCATGTCCGTCGAGCTCCGCAGG CGCGTCCAGCGCGACCGGCATCAAGCTCCCGGCGACGCTCGCGTTCGA CCACCCGACGCCGAGCGCTCGCGAGCAAGGTGCTCGCCGCGATCGTCC

TCCACGACGCGACCCCGCGCGCGCCCCCGCGGAGCTCGAGCGCCTC

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GAGGGGATGCTCTCGGCGATCTACGCGGACGAAGCGCTCCGCGACGACCT CACGGCGCGCCTCCGCGCCTTCCTGGACAAGCGCGCGGTCCGCACCGAAC 10 GCCCCGACGACGCCGCGTTCGCCGAGAAGCTCGGCTCCGCGAGCGCCGAC GAACTCATTCGCCTGATCGATCAGAAGCTCGGAGATCGCATCGATGTCGA CTCCACAGGAGCGAGACGCGCCTGCGTGCGACGGAAGAGAGGCGACATGA 15 GCCGATCGCCATCGTCGGCCTCCGGGCCGGGCGGGATCCACG ACCGCGACACGCTCTGGACGTTCCTCGAGGAGGGCCGCGACGCCATCGCG CCGATCCTCGCGAGCCGCTGGAACGCGGACGTACGACCTCGATCC 20 GGACGCCGTCGGCAAGAGCTACGTGCGCGACGCCGCCATGCTCGATCGCG 10 TCGACCTTTTCGACGCCGATTTCTTCGGGATCAGCCCGCGCGAGGCGAAG TACGTCGACCCGCAGCACCGCCTCTTGCTCGAGACGTCGTGGCAAGCGCT CGAGGACGCGGGGATTGTGCCGGCGTCGCTGCGAGACTCGAAGACCGGCG 25 TCTTCGTCGGCACGGGCGAGCGACTACGCGTTCCTCCAGAGCGATCGC GACGCCTCGGAGGCGTACGCGTTCATGGGGATGATCTCGTCGTCGCGGC 30 ACACGGCGTGCTCTCGTCGCTCGCGCTCCACCTCGCGTGCCAGTCG CTGCGTCAAGGCGAGTGCGACCTCGCGCTCGTCGCGGGTGTGCAGGTCAT 20 GCGACGGCGATCGAAGACGTTCTCGGCGAACGCCGACGGCTATGGCCGC 35 GAAAGGGCGCCCGATCCTCGCGGTGATCCGCGGCAGCGCGGTGAACCACG ACGGCACGTCGAGCGGGATCACGGTCCCGAACGGGCCCGCGCAGCAGAAG GTGCTCCGCGCCGCCGCCGACGACGCGCGGCCTTGTCCCCGCCGACGTCGA 40 25 CGTCGTCGAGTGCCACGGCACGGGGACCTCCATCGGAGG TGAACGCGCTCGCCGTCTACGGCGAGGGCGCCCCAAGGACCGCCCG CTGTTCCTGGGCGCGCTGAAGACCAACATCGGGCACCTCGAGTTCGCGTC 45 GGGCCTCGCCGCGCGAGAGATGGTCGCCTCCATGCGCCACGCGACCC TCCCCGCGACGCTGCACACGAGCCCGCTCAACCCGCTCGTCGACTGGGAC GCGCTCCCCGTGCGCGTCGTCGACGCCGCGCGCCCGTGGACGCCCCGCGA

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CCGCCGAGCCCGAGCCCACGACGCCGACGCCGCGCCTTCCGGCC AGCGCGCCTCCACGCGCACCTCGCGGGGCGCCCCGACGCGCGCTCGTCG GCCGTCGTCGCGGCGGATCGCGACGACGCTCCTCGGCGCGCTCGACGCGCT CGCGCGCGGGGGAGGCCCGGGGTCGGTCGCGAGCGCGATCCCCG CCGGCAGGGTCGTGTTCGTGTTCCCCGGCCAAGGCTCGCAGTGGGTCGGG ATGGCGCGCGCTCCTCGCGTCGTCGTGGTCTTCCGCGACGAGATCGC 10 GGCCTGCGAGCGCGCGCCGCGCACGTCGCCTGGTCGCTCGGCGCCG TTCTCCGGGGCGACGGCGACGCGCCTCCTCGGCCGCGTCGACGTC GTGCAGCCGGTCTTCGCCGTCATGGTCGCCCTCGCCGCGCTCTGGCG CTCGATCGGCGTCACGCCGACGCCGTCGTCGGGCACAGCCAAGGCGAGA TCGCCGCCGCCTACGTCGCCGGCGCCCTCTCGCTCGAAGACGCCGCCAAG 15 GTCGTCGCGCTGCGCGCACGAGCGCTCACGAAGATCGCGGGGCGCGGGGC GATGGCCGCCGTCGAGCTCGGCGCACGCGACACCGAGGCGCCCTCGCGC CGTTCGGCGACGCCATCGCGATCGCGGCGATCAACAGCCCGCGCGCCACG CTCGTCGCGGGCGACACGGACGCGATCGACGCGCTCGTCCGCGACCTCGA ${\tt GGCCGCGCAGATCTTCGCGCGGAAGGTGCGTGTCGACTACGCGTCGCACT}$ CGGCGCACGTCGAGGCGATCGAGCGCGAGCTCCTCGCGGATCTCGCGGGG ATCGAACCGCGCGGGGGCGCTGTGCCGCTTTACTCCGCGGTGACGGGCGC GAAGCTCGACGGGAACCGCCTCGACCCCGCGCATTGGTTCCGGAACCTGC GCTCGACAAAAACTTTGAGGACGCCACGCGCGCGCTCCACGACGACGGC CGCCGGGTATCCTCATNATCNNGGGCGTNCAGAGGAGTCGGTATTNCCCC 25 CCCCCGCCTTNCCCG,

or their complementary strands,

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(b) DNA-sequences which hybridise under stringent conditions to regions of DNA-sequences according to (a) encoding proteins 10 or to fragments of said DNA-sequences,

- (c) DNA-sequences which hybridise to the DNA-sequences according to (a) and (b) because of a degeneration of the genetic code,
- (d) allele variations and mutants resulting by substitution, 20 insertion or deletion of nucleotides or inversion of nucleotide segments of DNA-sequences according to (a) to (c), wherein the variations and mutants offer isofunctional expression products.
 - 15. Peptide encoded by a DNA sequence according to claim 14 selected from the group consisting of 15
- Seq ID No 121 >Contig17_001 828 amino acids MW=86259 D pI=5.60 numambig=1 MTVMATPGIFGEFSAQHAGAPDGRCKSFSSHANGAGWSEGAGIVLLERLSDARKNGHPVL $\verb|AIVRGSAVNQDGKSQGLTAPNGPAQERVIRDALASAGLAPADVDAVEAHGTGTTLGDPIE|$ 35 aralfatygaahakerplwlgslksnlghtqaaagiggvikmvlalqsgvlprtlhaasp SQHIDWSSGAIRLLTEEVPWKPGGSPRRAAVSSFGISGTNAHVVLEEAPRAAAGDDQAGE PARAPFAPPVPVLLSAKSDAALRAQAGKLHAHLAEHEDVALVDVAASLATTRSHFERRAA VVADDRAALLSALAALAEGRAGAGTVAGEALPPGKVAFVFPGQGSQWPSMARALLASSPA 40 25 FRAEIEACERALAPHVDWSLLAVLGGDEAHAAPMLERVDVVQPVLFAVMIALAATWRAAG VTPDAVVGHSQGEIAAAYVAGALSLEDAARVVALRSRAITKLAGRGAMSAVELTTAELEA rlaplgerlaiaainsphaalvsgdpgaidelvaelsgaqlfarkvrveyashsahveai 45 ERTMLEALDGIAPRPATVPLYSAVTGERLDGEALGAAHWYRNLRHTVRFEHATRALLDDG HRFFVEVSPHPVLTVALDETLSSIDGDATVVSSLRRDEGDLERFLLSAGELHARGHAIDW

GAFFAPLGARRVTLPTYAFQRERFWLDAGDASDDEDAAPGASAEETAFWRAIERGDVAAL 50

SDALHVADSGRRSALESLMPALSAWRRSRREQSTVGAWRYRVEWRPVSAASRGDVAGTWL VVAPAGVASDLASALAAALTERGADVVPLALEASDITDTGCRDRMSNVX

Seq ID No 122

5 >Contig18_002 502 amino acids MW=53019 D pI=6.83 numambig=1 FRXPDVHDRLANLVARRDYFYQLALRAAGTYVRGLVRAPHDGARPPAFAPRGAALVTGGT GALGAHVARWFARIGAEHIVLASRRGAAAPGAAALAEELSVLGARVTLVACDVPDREAVA GLVRNVKAGGATVRAVFHAGGAMHEAPVAAMRVEELADAIAVKARGAQHLQDVFAQRPLN AFVLFSSETGVWGGGRQGAYAAANAFLDALAEARRADGLAATSIAWGAWAGGGMLATDAE RRLKHRGVAPMDPELAVAALAHALDHAETCLAVADVDWARFAPSFASARPRPLLDELAEA RSALDALREPPDDARTAAGPEPASTERTTLAALPEGERHRHLLALVRTETAAVLGHADAS RVEPNRGFFDLGLDSLMSVELRRRVQRATGIKLPATLAFDHPTPSALASKVLAAIVLHDA TPRASPAAELERLEGMLSAIYADEALRDDLTARLRAFLDKRAVRTERPDDAAFAEKLGSA

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Seq ID No 123

SADELIRLIDOKLGDRIDVDRY*

SCONTIG18_010 840 amino acids MW=88062 D pI=5.74 numambig=6
MSTVTNDTLTEYLRRLTQELHRSETRLRATEERRHEPIAIVGLGLPFRGGIHDRDTLWTF
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VDPQHRLLLETSWQALEDAGIVPASLRDSKTGVFVGTGASDYAFLQSDRDASEAYAFMGM
ISSFAAGRLAFTLGLQGPALSIDTACSSSLVALHLACQSLRQGECDLALVAGVQVMSSPE
VFVLLSRTRALASDGRSKTFSANADGYGRGEGVVVLAVERLRDARAKGRPILAVIRGSAV
NHDGTSSGITVPNGPAQQKVLRAALDDARLVPADVDVVECHGTGTSIGDPIEVNALAAVY
GEGRPKDRPLFLGALKTNIGHLEFASGLAGVAKMVASMRHATLPATLHTSPLNPLVDWDA
LPVRVVDAARPWTRRDDGAPRRAGVTAIVEEAPAEPEPTTPDAAPALPAVPVLLSGKTDE
ALRAQAARLHAHLAGRPDARLVDIAASLATTRTHFDRRAAVVAADRDELLGALDALARGE
AGPGSVVASAIPAGRVVFVFPGQGSQWVGMARALLASSVVFRDEIAACERALAPHVAWSL
GAVLRGDGDEATLLGRVDVVQPVLFAVMVALAALWRSIGVTPDAVVGHSQGEIAAAYVAG
ALSLEDAAKVVALRARALTKIAGRGAMAAVELGARDTEARLAPFGDAIAIAAINSPRATL
VAGDTDAIDALVRDLEAAQIFARKVRVDYASHSAHVEAIERELLADLAGIEPRAGAVPLY

SAVTGAKLDGNRLDPAHWFRNLRSTKNFEDATRALHDDGRRVSSXSXAXRGVGIXPPRLX

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16. Recombinant expression vector which comprises a DNAsequence according to any of claims 1 to 10, 12 and 14.

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17. Procaryotic or eucaryotic cell which has been transfected or transformed with a DNA-sequence according to any of claims 1 to 10, 12 and 14 or with a recombinant expression vector according to claim 16.

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18. Cell according to claim 17, wherein the cell is derived from myxobacteria.

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15 19. Cell according to claim 17, wherein the cell is derived from a Sorangium strain.

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20. Cell according to claim 17, wherein the cell is derived from Sorangium cellulosum.

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21. Cell according to claim 17, wherein the cell is derived from a Streptomyces strain.

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22. Cell according to claim 17, wherein the cell is derived from Escherichia coli.

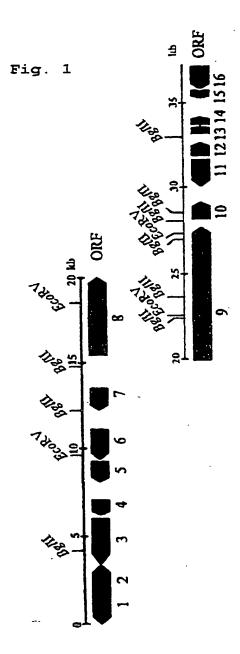
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23. Process for an enzymatic biosynthesis, mutasynthesis or partial synthesis of polyketide or heteropolyketide compounds, wherein a cell according to any of claims 17 to 22 is culti-

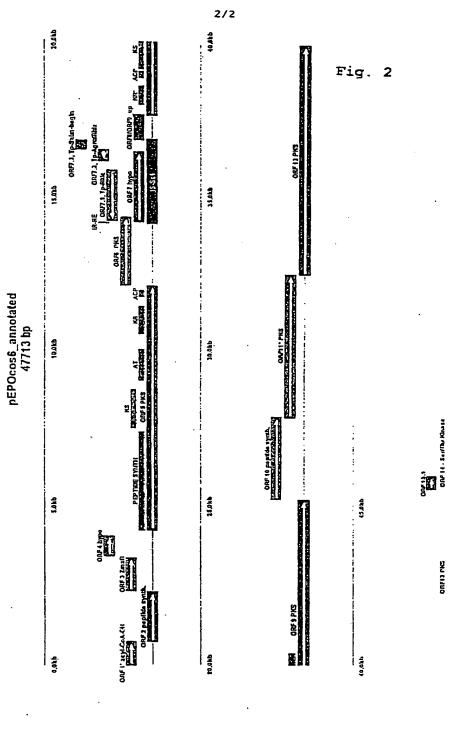
vated in a suitable culture medium and the polyketide or heteropolyketide compound is isolated from the medium.

24. Process according to claim 23, wherein the polyketide or

heteropolyketide compound is an epothilone.



Open reading frames found on pEPOcos6 region.



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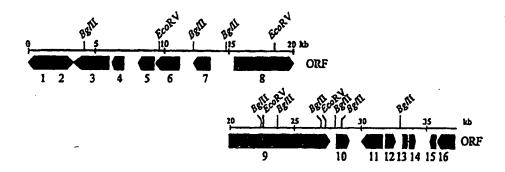
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[Continued on next page]

(54) Title: DNA SEQUENCES FOR ENZYMATIC SYNTHESIS OF POLYKETIDE OR HETEROPOLYKETIDE COMPOUNDS



(57) Abstract: The invention consists of: (1) cloned Sorangium cellulosum polyketide synthase (PKS) biosynthetic cluster DNA; and (2) the nucleotide sequence and predicted protein coding sequences of the cloned DNA. The invention can be used for, but not limited to: (a) increasing yields of PKS product in Sorangium cellulosum (e.g., by amplification or genetic modification of the epothilone gene cluster or its component parts); (b) increasing yields of polyketide product in a heterologous system by transfer of the epothilone gene cluster or its component parts, which may be followed by amplification or genetic modification of the PKS gene cluster or its component parts; (c) modification of the polyketide product chemical structure in either Sorangium cellulosum or a heterologous host (e.g., by genetic modification of the epothilone gene cluster or its component parts; and (d) for the detection of genes and gene products involved in making polyketides or related molecules in other organisms (e.g., by hybridization or complementation assays). DNA sequence and analysis is presented for the following cosmids and plasmids: A2 cosmid; the pEPOcos6 region (overlapping of pEPOcos6 and pEPOcos7); pEPOcos8 cosmid; A5 cosmid; Sau4 (10 kb plasmid).



(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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Inten Inal Application No PCT/US 99/23535

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CLASSIFICATION OF SUBJECT MATTER PC 7 C12N15/52 C12N A. CLASS C12N5/10 C12P17/06 C12N9/00 C12N15/63 C07K14/195 C12P17/18 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C07K IPC 7 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages 1.3-5.US 5 716 849 A (SCHUPP THOMAS ET AL) Χ 16,17, 10 February 1998 (1998-02-10) 22,23 18-21 abstract column 1, line 15 - line 23 column 4, line 8 - line 33 column 4, line 66 -column 5, line 40 example 1 -/--Patent family members are listed in annex. Further documents are listed in the continuation of box C. "T" later document published after the international filing date or priority date and not in conflict with the application but Special categories of cited documents: cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to filing date involve an inventive step when the document is taken alone document which may throw doubts on priority claim(s) or "Y" document of particular relevance; the claimed invention which is cited to establish the publication date of another cannot be considered to involve an inventive step when the document is combined with one or more other such docucitation or other special reason (as specified) O° document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. *P* document published prior to the international filing date but "3." document member of the same patent family later than the priority date claimed Date of mailing of the international search report Date of the actual completion of the international search 2 3. 10. 00 18 August 2000 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, CEDER 0. Fax: (+31-70) 340-3016

INTERNATIONAL SEARCH REPORT

Inter onal Application No
PCT/US 99/23535

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	<u> </u>
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SCHUPP T ET AL: "SORANGIUM CELLULOSUM (MYXOBACTERIUM) GENE CLUSTER FOR THE BIOSYNTHESIS OF THE MACROLIDE ANTIBIOTIC SORAPHEN A: CLONING, CHARACTERIZATION, AND HOMOLOGY TO POLYKETIDE SYNTHASE GENES FROM ACTINOMYCETES" JOURNAL OF BACTERIOLOGY, vol. 177, no. 13, July 1995 (1995-07), pages 3673-3679, XP000893003 WASHINGTON, DC ISSN: 0021-9193 the whole document	1,3-5, 16,17, 22,23
X	WO 93 13663 A (ABBOTT LAB) 22 July 1993 (1993-07-22) abstract	1,16,17, 21,23
A	WO 98 22461 A (BIOTECHNOLOG FORSCHUNG GMBH;GERTH KLAUS (DE); HOEFLE GERHARD (DE)) 28 May 1998 (1998-05-28) the whole document	2,24
P,X	BEYER S ET AL: "METABOLIC DIVERSITY IN MYXOBACTERIA: IDENTIFICATION OF THE MYXALAMID AND THE STIGMATELLIN BIOSYNTHETIC GENE CLUSTER OF STIGMATELLA AURANTIACA SG A15 AND A COMBINED POLYKETIDE (POLY) PEPTIDE GENE CLUSTER FROM THE EPOTHILONE PRODUCING STRAIN SORANGIUM CELLULOSUM SO CE90" BIOCHIMICA ET BIOPHYSICA ACTA. GENE STRUCTURE AND EXPRESSION, vol. 1445, no. 2, 14 May 1999 (1999-05-14), pages 185-195, XP000915670 AMSTERDAM ISSN: 0167-4781 the whole document	1-5
Ε	WO 99 66028 A (NOVARTIS ERFIND VERWALT GMBH; NOVARTIS AG (CH); SCHUPP THOMAS (CH)) 23 December 1999 (1999-12-23) the whole document	1-6,8, 16-24
E	WO 00 31247 A (KOSAN BIOSCIENCES INC) 2 June 2000 (2000-06-02) the whole document	1-6,8, 16-24

International application No. PCT/US 99/23535

INTERNATIONAL SEARCH REPORT

Box I Observati ns where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-5 and 16-24 partly and 6,8 completly
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-5 and 16-24 partly and 6,8 completly

Nucleic acid and polypeptide sequences involved in polyketide synthesis and related to cosmid A2 and their uses, where the sequences are seq id nos 1,3-34.

2. Claims: 1-5 and 16-24 partly and 7,9 completly

Nucleic acid and polypeptide sequences involved in polyketide synthesis and related to the pEPOcos6 region and their uses, where the sequences are seq id nos 2,35-70.

3. Claims: 1-5 and 16-24 partly and 10,11 completly

Nucleic acid and polypeptide sequences involved in polyketide synthesis and related to the pEPOcos8 region and their uses, where the sequences are seq id nos 71-88.

4. Claims: 1-5 and 16-24 partly and 12,13 completly

Nucleic acid and polypeptide sequences involved in polyketide synthesis and related to the cosmid A5 and their uses, where the sequences are seq id nos 89-118.

5. Claims: 1-5 and 16-24 partly and 14,15 completly

Nucleic acid and polypeptide sequences involved in polyketide synthesis and related to plasmid Sau4 and their uses, where the sequences are seq id nos 119-123.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter anal Application No
PCT/US 99/23535

Patent document cited in search report		Publication date		atent familý nember(s)	Publication date
US 5716849	A	10-02-1998	US	5639949 A	17-06-1997
		•	AU	695364 B	13-08-1998
			AU	2417895 A	04-01-1996
			BG	101107 A	28-11-1997
			BR	9507948 A	18-11-1997
			CA	2192366 A	14-12-1995
			CN	1152941 A	25-06 - 1997
		•	CZ	9603601 A	14-01-1998
			EΡ	0759078 A	26-02-1997
			HU	76534 A	29-09-1997
			WO	9533818 A	14-12-1995
•			JP	10501125 T	03-02-1998
			NZ	285166 A	27-04-1998
			PL	317998 A	12-05-1997
			SK	156996 A	06-08-1997
			US	6117670 A	12-09-2000
			US	5670350 A	23-09-1997
			US	5643774 A	01-07-1997
			US	5723759 A	03-03-1998
			US	5679560 A	21-10-1997
			US	5698425 A	16-12-1997
			US	5710031 A	20-01-1998
			US	5686282 A	11-11-1997
			US	5686283 A	11-11-1997
			US	5817502 A	06-10-1998
			ZA	9504686 A	08-12-1995
				9504000 A	
WO 9313663	Α	22-07-1993	CA	2100791 A	18-07-1993
			AU	665526 B	11-01-1996
			AU	1245092 A	03-08-1993
			EP	0626806 A	07-12-1994
WO 9822461	 A	28-05-1998	AU	5483798 A	10-06-1998
NO JOELTOI	^	20-03 1770	BR	9713363 A	25-01-2000
			CN	1237970 A	08-12-1999
			CZ	9901750 A	15-09-1999
			EP	0941227 A	15-09-1999
			NO	992338 A	14-05-1999
			PL	333435 A	06-12-1999
•			ZA	9710384 A	18-05-1999
			<i>L</i> n	7/10307 A	
	A	23-12-1999	ΑU	4611699 A	05-01-2000
WO 9966028	Α				40 00 000
WO 9966028	A	20 12 1777	US	6121029 A	19-09-2000
WO 9966028	A 		US	6121029 A	19-09-2006